
From: Wolinetz, Carrie (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=WOLINETZCDC9A]
Sent: 10/26/2016 5:59:21 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]; Hammersla, Ann (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=Recipients/cn=hammerslaa]
Subject: FW: [Invite] Meeting Request re: Xtandi
Attachments: 00.00.00 Meeting Request about Xtandi.pdf

From: Hudson, Kathy (NIH/OD) [E]
Sent: Wednesday, October 26, 2016 1:58 PM
To: Waitekus, Crystal (OS/IOS) <Crystal.Waitekus@hhs.gov>
Cc: Wolinetz, Carrie (NIH/OD) [E] <carrie.wolinetz@nih.gov>; Baker, Rebecca (NIH/OD) [E] <bakerrg@od.nih.gov>; Burklow, John (NIH/OD) [E] <BurklowJ@OD.NIH.GOV>; Hallett, Adrienne (NIH/OD) [E] <adrienne.hallett@nih.gov>; Schulke, Hilda (NIH/OD) [E] <schulkeh@od.nih.gov>
Subject: RE: [Invite] Meeting Request re: Xtandi

Hi Crystal,
I am happy to take this meeting and will engage others at NIH as needed. Once you respond, is the expectation that the group will reach out to my office directly?
Best,
Kathy

From: Waitekus, Crystal (OS/IOS)
Sent: Wednesday, October 26, 2016 1:47 PM
To: Hudson, Kathy (NIH/OD) [E] <Kathy.Hudson@nih.gov>
Subject: FW: [Invite] Meeting Request re: Xtandi

Kathy,

Good afternoon and I hope this finds you well!

We received the attached meeting request for Secretary Burwell last week and her Counselor Bobby Clark recommended you take the meeting in her stead.

She agreed with this recommendation and we hope you can accommodate a meeting with Paul Davis.

Please note OGA has also set-up a meeting with this group (HHS POC is Katie Kampf).

I will send a formal response on behalf of the Secretary and copy you.

Many thanks,

Crystal

Event:	**Meeting Request re: Exporting Xtandi**
Date:	No Specific Date
Location:	Washington, DC
Who issued invitation:	Paul Davis, Knowledge Ecology International
Notes:	He would like to follow-up with you about a request for the U.S. to exercise its rights to grant permission to manufacture enzalutamide to developing countries. This prostate

cancer drug is marketed as Xtandi by Astellas Pharma, however their prices deny access to almost everyone worldwide. This especially affects patients of African descent who have a severely disproportionate rate of mortality without access to this drug.

Recommendation:	**Decline per Bobby. He recommends Kathy Hudson with NIH take this meeting in your stead. OGA also has plans to have a staff-level meeting with this group in listening mode only. They agree with Bobby's recommendation.**

From: Waitekus, Crystal (OS/IOS)
Sent: Tuesday, October 18, 2016 2:05 PM
To: Clark, Robert (Bobby) (OS/IOS)
Subject: RE: [Invite] Meeting Request re: Xtandi

Perfect, thank you!

From: Clark, Robert (Bobby) (OS/IOS)
Sent: Tuesday, October 18, 2016 2:04 PM
To: Waitekus, Crystal (OS/IOS)
Subject: RE: [Invite] Meeting Request re: Xtandi

Kathy Hudson has been the person most involved in the Director's Office.

From: Waitekus, Crystal (OS/IOS)
Sent: Tuesday, October 18, 2016 2:03 PM
To: Clark, Robert (Bobby) (OS/IOS)
Subject: RE: [Invite] Meeting Request re: Xtandi

Great, thanks for the quick response. Anyone particular at NIH?

From: Clark, Robert (Bobby) (OS/IOS)
Sent: Tuesday, October 18, 2016 2:01 PM
To: Waitekus, Crystal (OS/IOS)
Subject: RE: [Invite] Meeting Request re: Xtandi

Hi Crystal … Not a marketing inquiry. This is an issue that they have been raising with NIH. I would recommend that she refer this meeting to NIH.

From: Waitekus, Crystal (OS/IOS)
Sent: Tuesday, October 18, 2016 1:59 PM
To: Clark, Robert (Bobby) (OS/IOS)
Subject: [Invite] Meeting Request re: Xtandi

Bobby,

We received the attached meeting request about the drug Xtandi this past week.

It might be more of a marketing inquiry, but Julie said to run it by you first.

Do you think it's worthwhile to include in her weekly Invite Doc?

Many thanks,

Crystal

Description

From: Paul Davis [mailto:pdavis@keionline.org]
Sent: Wednesday, October 12, 2016 10:01 AM
To: Paul Davis
Cc: Burwell, Sylvia M. (HHS/OS); Kolker, Jimmy (HHS/OGA); Bleimund, Emily (OS/OGA); James Packard Love
Subject: Re: Request for Mtg on Xtandi for Export to Developing Countries

Dear Colleagues,

A few of us would appreciate the opportunity to have a word with you on this. Please let us know of any availability in the next couple weeks.

Thank you.

—
Paul Davis • pdavis@keionline.org<mailto:pdavis@keionline.org>
Knowledge Ecology Int'l
+1 202 817 0129
Skype/IM: pdavisx

On Oct 5, 2016, at 11:47 AM, Paul Davis <pdavis@keionline.org<mailto:pdavis@keionline.org>> wrote:

[Apologies for partial subject line in previous email.]

5 October, 2016

The Honorable Sylvia Mary Mathews Burwell
Secretary, Department of Health and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201

Dear Secretary Burwell,

Your office has received an important letter from the Canadian company Biolyse Pharma, requesting that the United States exercise its rights to grant permission to manufacture enzalutamide for export to developing countries. The drug is marketed as Xtandi by Astellas Pharma.

Xtandi is an important drug—and one that was invented substantially with public funds. The prices set by Astellas deny access to almost everyone in need worldwide.

Advanced prostate cancer is a devastating disease--and one that is growing quickly in emerging economies. When this fact is coupled with the severely disproportionate rates of mortality documented in patients of African descent, we see an unacceptable status quo that requires a response. Fortunately, ready solutions are at hand.

Knowledge Economy International requests a meeting between you and your staff to discuss the Biolyse letter and move towards actions that can be taken to increase access to enzalutamide in developing countries. Is there a time in the coming weeks we can meet?

Thank you.

Paul Davis, Knowledge Ecology International

Enclosures: 28 Sept Letter to DHHS from Biolyse Pharma

CC: Amb Jimmy Kolker, Assistant Secretary for Global Affairs
Emily Bleimund, Director, Office of Trade and Health

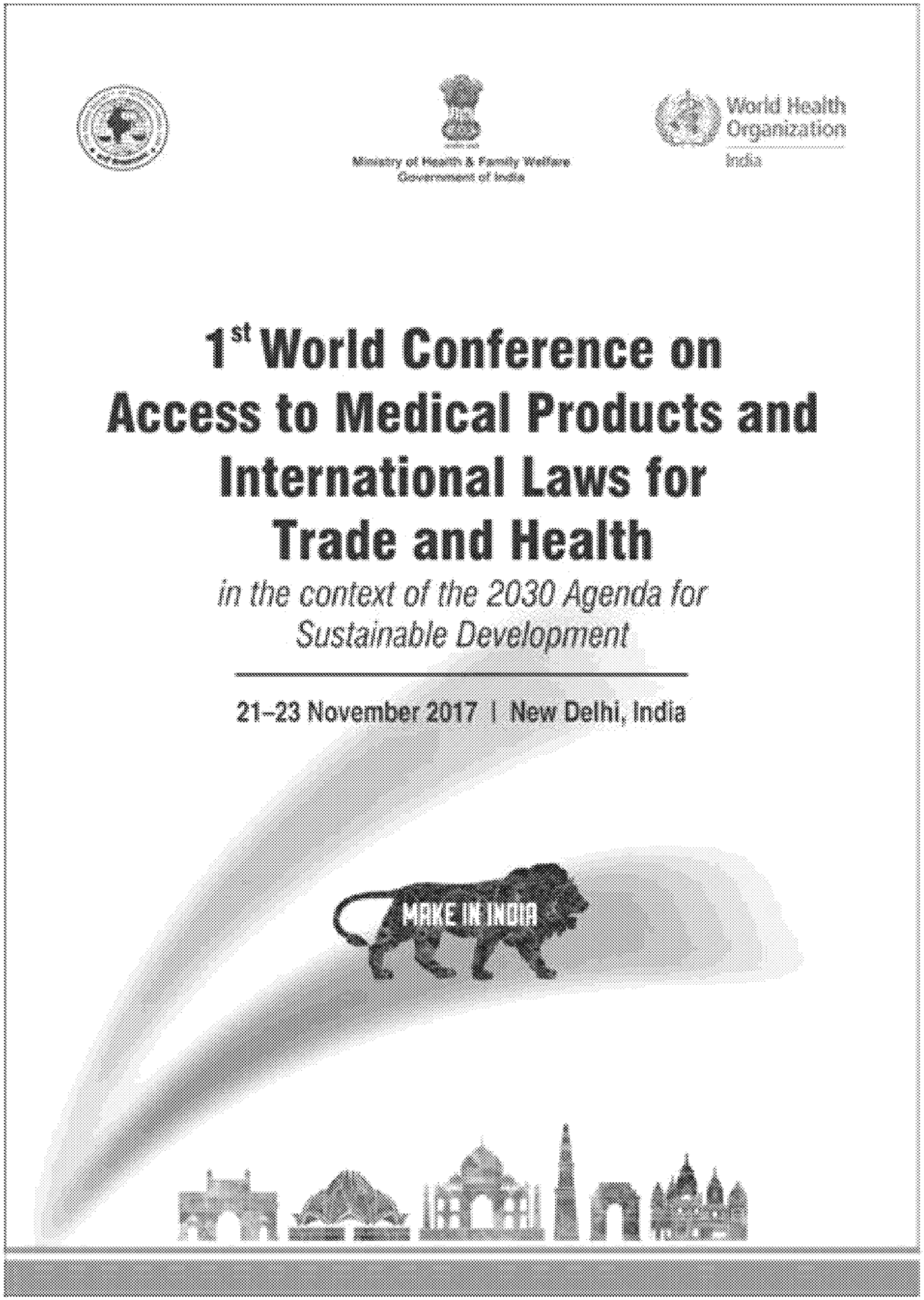
—
Paul Davis
pdavis@keionline.org<mailto:pdavis@keionline.org>
Knowledge Ecology Int'l
+1 202 817 0129
Skype/IM: pdavisx

From: Bleimund, Emily (OS/OGA) [Emily.Bleimund@hhs.gov]
Sent: 10/9/2018 7:52:08 AM
To: Verbois, Leigh (FDA/OC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c109e4eaabd14442a1ba1477a416d966-verboisl.fd]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: 1. Executive Summary 1st World Conference 21-23 November 2017.pdf - Sent from MaaS360
Attachments: 1. Executive Summary 1st World Conference 21-23 November 2017.pdf

THE INDIAN SOCIETY OF INTERNATIONAL LAW

Ministry of Health & Family Welfare

World Health Organization
India



Ministry of Health & Family Welfare
Government of India

World Health Organization
India

1st World Conference on Access to Medical Products and International Laws for Trade and Health

in the context of the 2030 Agenda for Sustainable Development

21–23 November 2017 | New Delhi, India

1ST WORLD CONFERENCE ON ACCESS TO MEDICAL PRODUCTS AND INTERNATIONAL LAWS FOR TRADE AND HEALTH

in the context of the 2030 Agenda for Sustainable Development

1st World Conference on Access to Medical Products and International Laws for Trade and Health
in the context of the 2030 Agenda for Sustainable Development
21-23 November 2017 | New Delhi, India
MAKE IN INDIA

Ministry of Health & Family Welfare, Government of India, Indian Society of International Law and World Health Organization Country Office for India

Ministry of Health & Family Welfare

World Health Organization
India

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Acknowledgements

Access to medicines is a critical factor for success of the 2030 Sustainable Development Agenda (SDG Agenda) that aims to ensure healthy lives and promote well- being of all people of all ages. The main objective of the Conference is exchange of knowledge and to expand understanding on contemporary issues in international trade laws and research and innovation for access to medical products to achieve SDG 2030 agenda.

The World Health Organization would like to thank the following for their support and contribution to the 1st World Conference on Access to Medical Products and International Laws for Trade and Health in the Context of the 2030 Agenda for Sustainable Development:

☐ Ministry of Health and Family Welfare, Government of India
☐ Indian Society of International Law
☐ World Health Organization
☐ Translational Health Science and Technology
☐ Biotechnology Industry Research Assistance Council
☐ Indian Council of Medical Research
☐ Research & Innovation Systems in Developing Countries
☐ Ministry of Science and Technology
☐ Ministry of Chemicals and Fertilizers
☐ Ministry of Commerce and Industry
☐ Ministry of Law and Justice
☐ Ministry of External Affairs
☐ Ministry of Micro Small and Medium Enterprises
☐ Ministry of Electronics & Information Technology
☐ Ministry of Culture, Government of India

Overall Leadership and Guidance from Ministry of Health and Family Welfare

☐ Ms Preeti Sudan, Secretary, Ministry of Health and Family Welfare, Government of India
☐ Dr RK Vats, Additional Secretary, Ministry of Health and Family Welfare, Government of India

Organizing Committee:

☐ Mr Sudhir Kumar, Joint Secretary, Ministry of Health and Family Welfare, Government of India - Chairman (Working Group)
☐ Dr Madhur Gupta, Technical Officer-Pharmaceuticals, WHO Country Office for India
☐ Mr DN Sahoo, Deputy Secretary, Ministry of Health and Family Welfare, Government of India
☐ Mr RG Singh, Under Secretary, Ministry of Health and Family Welfare, Government of India
☐ Dr Eswara Reddy, Joint Drugs Controller India, CDSCO, Government of India

Conference Secretariat:

World Health Organization

☐ Dr Manisha Shridhar, Regional Advisor, Intellectual Property Rights & Trade and Health, WHO SEARO
☐ Dr Madhur Gupta, Technical Officer-Pharmaceuticals, WHO Country Office for India
☐ Ms Preeti Kharb, Consultant, WHO Country Office for India
☐ Ms Neha Juneja, Consultant, WHO Country Office for India

The Indian Society of International Law*:*

☐ Dr SK Verma, Secretary General
☐ Mr Vinai Kumar, Associate Professor
☐ Ms Parineet Kaur, Assistant Professor

Inputs received from World Health Organization:

☐ Dr Henk Bekedam, WHO Representative to India
☐ Dr Prakin Suchaxaya, Coordinator, Health Systems, WHO India
☐ Dr Hilde Renne Susanne De Graeve, Team Leader, Health Systems, WHO India
☐ Ms Michele Yvone Vanderlanh Smith, WHO Country Office for India
☐ Dr Sue Hill, Director, Essential Medicines and Health Products, WHO, HQ

Grateful for overall Support:

Ministry of Health and Family Welfare and Ministry of Science and Technology:

☐ HE Mr JP Nadda, Honouable Union Minister, Ministry of Health and Family Welfare, Govt. of India
☐ HE Mr Ashwini Kumar Chaubey, Hon'ble Minister of State, Health & Family Welfare, Govt. of India
☐ HE Ms Anupriya Patel, Hon'ble Minister of State, Health & Family Welfare, Government of India
☐ Dr Soumya Swaminathan, Secretary, Department of Health and Research & Director General, Indian Council of Medical Research, Government of India
☐ Dr Gagandeep Kang, Executive Director, Translational Health Science and Technology Institute, India
☐ Dr Renu Swarup, Senior Adviser, Department of Biotechnology (DBT) and Managing Director, Biotechnology Industry Research Assistance Council (BIRAC)

National Institution for Transforming India (NITI) Aayog, Government of India:

☐ Dr VK Paul, Member, NITI Aayog

The Indian Society of International Law:

☐ Dr EMS Natchiappan, President, Indian Society of International Law

World Health Organization: Dr Poonam Khetrapal Singh, Regional Director, WHO SEARO

1st World Conference on Access to Medical Products and International Laws for Trade and Health in the Context of the 2030 Agenda for Sustainable Development

21-23 November 2017

Executive Summary

I. Introduction

The Ministry of Health & Family Welfare, Government of India, Indian Society of International Law (ISIL) with the support of WHO organized the **"1st World Conference on Access to Medical Products and International Laws for Trade and Health in the Context of the 2030 Agenda for Sustainable Development".** The conference was a sequel to the side event on the subject hosted on 24 May 2017 of the 70th World Health Assembly.

The Sustainable Development Goals are the first ever comprehensive globally-agreed development plan for our entire planet. They are the world's to-do list for a fairer, safer and healthier world by 2030. The health goals in the SDGs build on the unfinished business of the MDG era (such as on HIV, tuberculosis and malaria) and adds new targets, such as non-communicable diseases, universal health coverage. Trade and globalization have contributed to international and national movement in medical, food and health products across boundaries resulting in new challenges in the public health spectrum.

The United Nations (UN) High Level Report on access to medicines is proposed to be discussed in a special session in the UN 2018. The Conference in New Delhi enabled deeper discussions for development of a holistic view on access to medicines (including all medical products: medicines, vaccines, devices, and diagnostics).

The present overarching ambit of the SDG agenda and the significant role of international engagements particularly trade and contemporary political developments in national countries make it imperative to engage for tangible solutions. Of the 17 SDGs, Good health and well-being finds direct mention in Goal 3. The latter however, is a prerequisite for almost all other SDG goals. Universal health coverage and the interlinked agenda of access to medicines, is also one of the regional flagship priorities in the WHO South East Asia Region.

II. Objective

The main objective of the Conference was to exchange knowledge and expand understanding on contemporary issues in international trade laws and research and innovation for access to medical products to achieve SDG 2030 agenda.

III. Specific Objectives were:

1. Engage with a wide set of stakeholders in structured debate on access to medicines and medical products and trade agreements for upcoming international discussions in the context of SDGs.
2. Promote pragmatic responses to contemporary policy issues on research and innovation landscape and the paradigm shift needed in the changing innovation landscape for medical products and health technologies.
3. Provide recommendations for possible policy coherence on international trade laws and health, including intellectual property covenants for access to medical products

IV. Thematic areas of the Conference

The following three thematic areas were covered:

A. **Access to Medical Products**- the sub themes were:

1. Access to Medical products
2. Recommendations of the UN High Level Report on access to medicines
3. Regulatory dimensions to address access for quality, efficacious, safe and affordable medical products including cancer, hepatitis C, etc.
4. Use of Internet and Information Technology for accessing medical and health products (including online pharmacies)

B. **Innovation and Research & Development for moving towards SDGs**- the sub themes were:

1. Role of Innovation and R&D for Access to medical products, Competition law for Access to Medicines and health products, Bio-technological products, Patents as a tool of innovation
2. Access to Medical products (new/innovative Medical/ health products/ disease and dosage regimens), Infectious disease control (New initiatives for R&D (Coalition for Epidemic Preparedness Innovation (CEPI) for development of vaccines for infections of epidemic potential
3. New technologies providing innovative solutions for healthcare, fostering local production

C. **Intellectual Property Rights and Trade for SDGs in the context of Access to Medical Products**- the sub themes were:

1. International legal framework for access to medicines in the context of R&D and innovation – TRIPS, patent law, competition laws, Right to Health etc.
2. Patent and Trademarks in standard setting in medical products
3. Health-related provisions in Free Trade Agreements and Regional Trade Agreements in the context of medical products

V. Expected Outcomes

The expected outcomes from the conference were to:

1. Engage with a wide set of stakeholders, on critical issues of innovation, trade and access to medicines for upcoming international discussions on the UN High Level Report on access to medicines for 2018 Executive Board of WHO
2. Explore strategies to promote innovation and identify linkages between international trade and health policy for access to medical products to achieve SDGs
3. Provide recommendations for improved policy coherence on international trade and health, intellectual property for access to medical products taking into account globally negotiated commitments.

VI. Sessions Details

A total of 15 Sessions were held as follows:

- 4 Plenary sessions
- 8 Parallel sessions

- 3 Wrap-Up sessions for collating all recommendations
- 17 Chairs, 12 Co-Chairs, 31 Lead Discussants, and 59 Panelists from various countries and organizations including Ministry Officials, academia, industry, inter-governmental organizations and civil societies.

Subjects covered in Four Plenary Sessions

- Plenary Session 1- UN High Level Panel on Access to Medicines in the context of SDGs
- Plenary Session 2- Role of Innovation, Research and Development for Medical Products
- Plenary Session 3- Fostering Local Production, Technology Transfer and Market Entry Barriers for Medical Products
- Plenary Session 4- TRIPS, UN High Level Panel Report and Benefit sharing for access to medical products

Subjects of Eight Parallel Sessions

- Parallel Session 1- Regulatory Pathways for safe, quality, efficacious and affordable medical products including in emergencies to achieve SDG goals
- Parallel Session 2- Affordability and Fair Pricing of Medical Products
- Parallel Session 3- Infectious Disease Control: What are the Pathways to Technology Development and Access to Medical Products
- Parallel Session 4- Alternative Models of R&D-Industry-Academia Collaborations
- Parallel Session 5- Achieving SDGs: Use of Information and Communications Technology (ICT) Initiatives including in Trade Agreements
- Parallel Session 6- Patents , Intellectual Property, Price Control and Competition Law in Access to Medicines
- Parallel Session 7- WTO Trade Agreements influencing Health Products– Context SDGs
- Parallel Session 8-Achieving SDGs: Regional Agreements, Challenges(TRIPS plus Agreements) and Access to Medical products

A summary of the outcomes from each of the Plenary and Parallel sessions follows. The topics covered by the Speakers: Chairs, Co-Chairs, Lead discussants and Panelists is outlined (in italics) in the sessions brief to specify the subjects covered by them.

A total of 142 recommendations emerged for promoting access to medical products to achieve the 2030 SDG agenda from the conference. The recommendations were for national governments, WHO and other international organizations.

Recommendations in Brief	
National Governments	**70**
WHO/ International organizations	**68**
United Nations	**4**
Total	**142**

Plenary Session 1: UN High Level Panel on Access to Medicines in the context of SDGs

Chairs:

1. **Dr VK Paul**, Member, NITI Aayog, Government of India
2. **Ms Preeti Sudan**, Secretary, Health, Ministry of Health and Family Welfare, Government of India
3. **Dr Soumya Swaminathan**, Secretary, Department of Health and Research & Director General, Indian Council of Medical Research, Government of India

Lead discussants

1. **Ambassador Dr Virander Paul**, Deputy Permanent Representative of India to the United Nations- *Access to Medicines: A Perspective from the Permanent Mission of India to the United Nations*
2. **Ms Ruth Dreifuss**, Co-chair, UN High Level Panel on Access to Medicines; Former President, Swiss Confederation, Geneva- *Governance, Accountability and Transparency*
3. **Dr Jorge Bermudez,** Senior Researcher in Public Health, National School of Public Health, Fiocruz, Ministry of Health, Brazil- *Intellectual Property Laws and Access to Health Technologies*
4. **Dr Mandeep Dhaliwal,** Director-HIV, Health and Development Group, United Nations Development Program, USA- *New Incentives for Research and Development of Health Technologies*

Panelists

1. **Dr Peter Beyer**, Senior Advisor, Department Of Essential Medicines and Health Products, World Health Organization, Geneva- *WHO's work on Access and Innovation*
2. **Ms Maria Lorena Di Giano**, Executive Director, Fundacio Grupo Efecto Positivo and General Coordinator of RedLam, Argentina- *Intellectual Property Laws and Access to Health Technologies*
3. **Professor Anthony D So**, Professor of the Practice and Director, IDEA (Innovation+Design Enabling Access) Initiative, Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA- *Innovation and Access to Health Technologies*
4. **Dr Mohga Kamal Yanni**, Senior Health and HIV Policy Adviser, Oxfam GB, UK- *Health Policy and Programming*
5. **Mr Anand Grover**, Former UN Special Rapporteur and Member- Expert Advisory Group, UN High Level Panel on Access to Medicines, India- *International Trade Rules in the Context of Human Rights to Health*

The **objective of the session** was to enable deeper discussions and a take holistic view on access to medicines (including all medical products: medicines, vaccines, devices, diagnostics) and the issues and recommendations made in the UN High Level Panel Report.

The topics addressed in "**Access to Medicines (and Medical products) to achieve SDGs**" are as follows:

1. Governance, Accountability and Transparency
2. Intellectual Property Laws and Access to Health Technologies
3. New Incentives for Research and Development of Health Technologies
4. Health Technology Innovation and Access
5. WHO's position and next steps on UN HLP
6. New Incentives for Research and Development of Health Technologies
7. Intellectual Property Laws and Access to Health Technologies
8. Innovation and access to health technologies
9. Health policy and programming

Recommendations:

Recommendations for National Governments

1. Ensure coherence at the multilateral, regional and national levels so that all policies advance the right to health, the right to benefit from scientific progress, and to achieve the Sustainable Development Goals, including SDG 3.
2. Establish national level inter-ministerial bodies to co-ordinate laws policies and practices that may impact on health technology innovation and access.
3. Review access to health technologies and make them publicly available in the countries in the light of human rights principles and States' obligations to fulfil them, with assistance from the Office of the UN High Commissioner for Human Rights.
4. Enable disclosure of the costs of Research and Development (R&D), production marketing and distribution by manufacturers and distributors of their products.
5. Enable disclosure of public funding received in development of health technologies such as tax credits, subsidies and grants.
6. Make publicly available unidentified data on all completed and discontinued clinical trials regardless of whether their results are positive, negative, neutral or inconclusive
7. Establish and maintain publicly accessible databases with patent information status and data on medicines and vaccines.
8. Strengthen with appropriate national interventions the international mechanism of WHO Clinical Trials Registry Platform
9. Increase current levels of investment in health technology innovation to address unmet health needs.
10. Use Trade-Related Aspects of Intellectual Property Rights (TRIPS) flexibilities and take into account the impact on public health of TRIPS plus provisions when negotiating any Free Trade Agreements (FTAs).

Recommendations for WHO/ International Organizations

1. Annex the report of "1st World Conference on Access to Medical Products and International Laws for Trade and Health in the Context of the 2030 Agenda for Sustainable Development, 21-23 November 2017, New Delhi, India" in the Executive Board 2018 agenda on Access to medicines for forthcoming WHA .
2. Promote adoption of mechanisms to mobilize resources to build sustainable, coherent solutions for financing of health research and development (R&DS), to advance the right to

health and the right to benefit from scientific progress. Such mechanisms should integrate public health safeguards, as summarized in WHA 66.22 in order to find solutions to the unmet medical needs which ensure a fair public return for public investments, and enable the delinking of R&D incentives from drug prices for affordable and universal access.

3. WHO draft general programme of work 2019-2023 should give adequate focus on Access to medical products.
4. WHO should establish and maintain a database of prices of patented, generic and biosimilar medicines in countries where they are registered.
5. Create easily searchable patent database, periodically updated and consolidated in collaboration with Member States, patent owners and other stakeholders.
6. R&D funders to test new business models, particularly of delinkage including with companies engaged in early stage research and address obligations of access and stewardship.
7. Use the G20 and G77 platforms for collective actions on access to medical products and for Antimicrobial resistance (AMR).

Recommendations for the United Nations

1. UN Secretary-General should establish an independent review body (with broad membership from various constituencies) tasked with assessing progress on health technology innovation and access.
2. UN Secretary General should establish an inter-agency task force to increase coherence between multilateral organizations working on health technology innovation and access.
3. UN Secretary General should convene a UN General Assembly Special session on health technology innovation and access in 2018.
4. Develop next steps to UN Human Rights Council adopted Resolution 26/9 in June 2014 that mandated to develop "an international legally binding instrument on transnational corporations (TNCs) and other business enterprises with respect to human rights".

Parallel Session 1: Regulatory Pathways For Safe, Quality, Efficacious and affordable Medical Products including in Emergencies to Achieve SDG Goals

***Chair:* Dr RK Vats**, Additional Secretary, Ministry of Health and Family Welfare, Government of India

***Co-chair:* Dr Renu Swarup**, Senior Adviser, Department of Biotechnology and Managing Director, Biotechnology Industry Research Assistance Council- Biopharma Mission, India

Lead discussant:

1. **Dr Gagandeep Kang**, Executive Director, Translational Health Science and Technology Institute, India- *Regulatory Pathways for Vaccines and New Models (Including CEPI) to Achieve SDG Goals*
2. **Dr GN Singh**, Drugs Controller General (India), Central Drugs Standard Control Organization, India- *Regulatory Updates in India*
3. **Dr Stephen B Kennedy**, Coordinator for EVD Research, Incident Management System, Ministry of Health, Liberia- *Regulatory Pathways in Emergencies – From Clinical Trials to Field*

Panelists:

1. **Dr Anban Pillay**, Director, National Department of Health, South Africa- *Innovative Medicine Supply Models for Access to Affordable Medicines*
2. **Dr Anil Koul**, Director, CSIR-Institute of Microbial Technology, India- *New Drug Development*

for Tuberculosis

3. **Dr Jorge Bermudez**, Senior Researcher in Public Health, National School of Public Health, Fiocruz, Ministry of Health, Brazil- *Health Technology, Local Production and Innovation Including APIs*
4. **Ms Leena Menghaney**, Head- South Asia, Access Campaign, Medecins Sans Frontieres, India- *Challenges to Affordable Medical Products*
5. **Dr Taslimarif Saiyed**, CEO & Director, Centre for Cellular and Molecular Platforms, Department of Biotechnology, India- *Developing and Establishing High End Technologies*

The objective of this session was to discuss the ways in which the national regulatory systems can address ever-increasing complexities of medical product supply chains. The steps to enable shorter, transparent and more predictable regulatory pathways for newer medical products including in emergencies were also covered.

The following topics were taken up:

1. Regulatory Pathways for vaccines and new models (including *Coalition for Epidemic Preparedness Innovations -CEPI- the* Global partnership launched to prevent epidemics with new vaccines) to achieve SDG goals
2. Regulatory updates in India
3. Regulatory Pathways in emergencies- from clinical trials to field
4. Innovative medicine supply models for access to affordable medicines
5. Health technology, local production and innovation including Active Pharmaceutical Ingredients (APIs)
6. Challenges to affordable medical products

Recommendations:

Recommendations for National Governments

1. Build on existing regulatory harmonization/alignment efforts, WHO R&D Blueprint, WHO Pre-qualification (PQ) collaborative and joint review processes, South East Asia Regulatory Network (SEARN), Global Antibiotic Research and Development Partnership (GARD-P), African Vaccine Regulatory Forum (AVAREF), African Medicines Regulatory Harmonization initiative (AMRH), Pan-American Network for Drug Regulatory Harmonization (PANDRH) ASEAN-Network for Drugs, Diagnostics, Vaccines, and Traditional Medicines Innovation (ASEAN-NDI), International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH), European Medicines Agency's Article 58 procedure.
2. Develop regulatory mechanisms for coordination, cooperation and reliance among various stakeholders working in health sector to facilitate access of healthcare to the population at national and international levels.
3. Track patent working by the holder to enable non-registration to be used as a ground for non-working of the patent on new drugs leading to necessary government action.
4. Make candidates available (pre-final licensure) to most at risk populations (including first responders) via appropriate regulatory mechanism(s), if needed during an outbreak.
5. Explore new treatment options for diseases such as Tuberculosis including single pill regimens.
6. Promote new collaborative mechanisms including using TRIPS flexibilities for enhanced access to newer medical products for diseases specific to certain countries such as for access to bedaquiline, delamanid, Hepatitis, oncology medicines.

Recommendations for WHO/International Organizations

1. Outline procedures for clinical research in emergency situations including clinical trials, speedy ethics committee and regulatory approvals.
2. WHO to take forward the global regulatory optimization and alignment envisaged in CEPI, assist product developers to better understand the challenges of regulatory and ethics

processes in the absence of an outbreak.

3. Clarify regulatory and ethical issues surrounding the use of stockpiled products during outbreaks.
4. Assist national governments to develop coordination, cooperation, reliance regulatory mechanisms among various stakeholders working in health sector for facilitating access of healthcare to the population at national and international levels.
5. Assist national governments and international agencies to explore new treatment options for diseases such as Tuberculosis including single pill regimens.
6. Assist national governments to facilitate new collaborative mechanisms including using TRIPS flexibilities for enhanced access to newer medical products for diseases specific to certain countries such as for access to bedaquiline, delamanid, Hepatitis, oncology medicines.
7. Select study designs judiciously to provide best possible answers at conclusion of studies for global public health consumption.
8. Leverage community engagements for successful product development initiatives including in outbreaks.

Parallel Session 2: Affordability and Fair Pricing of Medical Products

***Chair:* Mr Jai Priye Prakash**, Secretary, Department of Pharmaceuticals, Ministry of Chemicals and Fertilizers, Government of India

***Co-Chairs:* Dr Henk Bekedam**, WHO Representative to India, **Mr Bhupendra Singh,** Chairman, National Pharmaceutical Pricing Authority, Government of India

Lead discussants:

1. **Professor Fatima Suleman**, Discipline of Pharmaceutical Sciences, University of Kwazulu-Natal, South Africa- *Creating a Balance Between Affordable Prices and a Sustainable Pharmaceutical Industry*
2. **Dr Sham Mailankody**, Memorial Sloan Kettering Cancer institute, USA- *Research and Development Costs in Bringing Medical Products to Market*
3. **Dr Andrew Rintoul**, Scientist, Pricing & Health Technology Assessment, World Health Organization, Geneva- *Fair Pricing Mechanisms for Public Health Systems in Developing Countries*

Panelists:

1. **Ms Michelle Childs**, Head of Policy and Advocacy, Drugs for Neglected Diseases (DNDi), Latin America- *Innovation using open Knowledge Principles including WHO Open Knowledge Demonstration Projects*
2. **Mr James Love**, Director, Knowledge Ecology International, USA- *Proposals for Expanding the Production of Knowledge as a Public Good*

The objective of this session was to explore policy options on fair pricing of medical products for Universal Health Coverage (UHC) in the context of the SDG 2030 Agenda.

The following topics were discussed:

1. Creating a balance between affordable prices and a sustainable pharmaceutical industry
2. Research and Development (R&D) costs in bringing medical products to Market
3. Fair pricing mechanisms for public health systems in developing countries
4. Promoting transparency in pricing of medical products
5. Price Control of medical products in India

6. Pharmaceutical Policies: Promoting affordability and fair pricing of medical products
7. Innovation using open knowledge principles including WHO open knowledge demonstration projects
8. Proposals for expanding the production of knowledge as a public goods

Recommendations:

Recommendations for National Governments

1. Examine to end tariffs and taxes on essential medicines to improve affordability.
2. Address unreasonable markups on medical products throughout the supply chain, also using information technology to create transparency and publicly report markups.
3. Develop alternate models to fund R&D learning from UNITAID example that receives certain funds from airline taxes or levies.
4. Focus on "reasonable bounds" of pricing for transparency and assure sustainability of industry to advance the practice of medicine and contribute to achieving universal access.
5. Collaborate with other payers to increase purchasing power for access to medical products by negotiations such as in initiatives BeNeLuxA.
6. Develop open collaborative models and make R&D more efficient, quicker and cheaper.
7. Ensure knowledge is made freely and widely available by applying conditions to public funding for R&D that require pro public health patenting and licensing practices (e.g. publication, non-exclusive licensing, donations of IP, patent pools, transparency on research data, clinical trial data -negative and positive).
8. Negotiate a Code of Principles for Biomedical R&D.
9. Provide for sufficiently detailed disclosure (including outlays on each trial) of R&D costs and R&D subsidies for every regulated medical technology.
10. Fully support and fund WHO's normative and technical functions.

Recommendations for WHO/International Organizations

1. Consider drafting and conforming to an agreement to avoid the complexities and challenges of R&D treaty ratification and modification.
2. Provide technical assistance to Member States for public procurement mechanisms, best procurement practices, increased transparency on pricing, inputs in the value chain and on production of medical products.
3. Focus on incentives for funding priority R&D and not limit benefits of global cooperation to developing countries.

Plenary Session 2: Role of Innovation, Research and Development for Medical Products

Chair: Ms Aradhana Johri, Former Secretary Department of Pharmaceuticals, Ministry of Chemicals and Fertilizers, Secretary of Finance (Disinvestment); Former Additional Secretary, Ministry of Health & Family Welfare, GOI

Co-chair: Dr Gagandeep Kang, Executive Director, Translational Health Science and Technology Institute, India

Lead discussants:

1. **Dr Renu Swarup**, Senior Adviser, Department of Biotechnology (DBT) and Managing Director, Biotechnology Industry Research Assistance Council (BIRAC)- Biopharma Mission, India- *Bio Pharma Mission: Enabling Environment for Industry Academia Collaboration from Discovery Research to Development for Biopharmaceuticals*

2. **Dr Madhur Gupta**, Technical Officer-Pharmaceuticals, WHO India- *Research and Development and access to Medical Products: Thematic Issues in WHA Resolutions and UNHLP*
3. **Dr Surinder Singh**, Director, National Institute of Biologics (NIB), India- *WHO R&D Blue Print: Way Forward*

Panelists:

1. **Mr Ed Whiting**, Director of Policy and Chief of Staff, Wellcome Trust UK- *Supporting Response to Epidemics and Antimicrobial Resistance*
2. **Dr Suman Rijal**, Executive Director, Drugs for Neglected Diseases (DNDi), India- *Global Successful Models of PDPs in R&D*
3. **Dr Nilima Kshirsagar**, National Chair of Clinical Pharmacology, Indian Council of Medical Research, India- *Clinical Trials Landscape in R&D*
4. **Professor Anthony D So**, Professor of the Practice and Director, IDEA (Innovation+Design Enabling Access) Initiative, Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA- *Grants and Co-Operative Agreements with Academic Institutions in Promoting R&D in Public Health*

The objective of the session was to identify the gaps in R&D and opportunities and define priorities for investments, priority setting and coordination in R&D including WHO R&D Blueprint.

The topics addressed in **"Role of Innovation, Research and Development for Medical Products"** are:

1. Bio Pharma Mission: Enabling environment for Industry Academia Collaboration from discovery research to development for biopharmaceuticals
2. Enabling regulatory landscape for medical devices and diagnostics: alliances, networks and coalitions
3. Research and development and access to medical products: thematic issues in WHA resolutions and UNHLP
4. WHO R&D Blue Print: Way Forward
5. Funding R&D through portfolio development for health care innovations
6. Global successful models of PDPs in R&D
7. Clinical Trials landscape in R&D
8. Grants and Co-operative agreements with academic institutions in promoting R&D in public health

Recommendations:

Recommendations for National Governments

1. Develop concerted action with the ministries of Science and Technology, Indian Council of Medical Research, Ministry of Chemicals and Fertilizers, Ministry of Commerce and Industry, Ministry of Law and Justice, Ministry of External Affairs, Ministry of Micro Small and Medium Enterprises, Ministry of Electronics & Information Technology and Ministry of Health on the access agenda for health for all.
2. Adapt the R&D blueprint in India and South East Asia Region for sustainable efforts for R&D for newer medical products including antibiotics in collaboration with the science and health ministries.
3. Encourage use-inspired discovery research - promote innovation and R&D for development of affordable products for Indian and global market, support strong technology platforms, create network of clinical sites and testing facilities.
4. Promote commercialization of technology by building translational capacity, support business incubation infrastructure, technology validation, scale-up infrastructure, nurture

bio-entrepreneurship and build technology repositories.

5. Generate biotech products, processes and technologies to enhance efficiency, productivity, affordable health and wellness.
6. Create an enabling environment for next generation product innovation through global and national alliances and redesigning governance models for focused, mentored, high quality product development.
7. Develop early consultation mechanisms with regulatory agencies for product development and use to ease market approval for products.
8. Develop innovative new technology enabled service delivery access models and relate geographical accessibility to medical products.

Recommendations for WHO/ International Organizations

1. Allocate adequate resources for achieving Global strategy and plan of action on public health, innovation and intellectual property (GSPA) outcomes, including the results in the programme review and Consultative Expert Working Group (CEWG) for achieving SDG 2030 goals.
2. Track progress on the GSPA and follow up resolutions including the CEWG Report on an annual basis.
3. Leverage regional regulatory networks such as South East Asia Regulatory Network (SEARN) for building cross linkages with regulatory and access agenda.
4. Build consortiums of partners to move innovation to scale (in-country & global network of research entities) and establish inclusive development models.
5. Build proficiency in intellectual property support and management.
6. Create a global network of experts/mentors/ advisors to work and partner for enhancing product innovation and bring together isolated Centers of Excellence.
7. Integrate cross platform technologies for application in other disease areas and utilization in other programs.
8. Strengthen entrepreneurial ecosystem and build regional competencies and enhanced bio-clusters ecosystem.
9. Leverage the Ebola learnings of WHO to consider adaptive R&D blueprint- call for action for devices, diagnostics, medicines and vaccines.
10. Revisit Global Clinical Trials requirements and abbreviated clinical trials model with risk based approach followed by risk minimization and post marketing plan in place.
11. Support public funded early drug development stage joint collaboration with academia, regulators and leverage Product Development Partnerships Models, CEPI, Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X), Global Antibiotic Research and Development Partnership (GARDP), Global Health Innovative Technology (GHIT).
12. Deliver value for money by offering the right amount of reward for the right products, and not ‘paying twice’ and ensuring access using mechanisms such as patent pooling.
13. Support good antibiotic stewardship by de-linking the profitability of a product from the volume sold, and through responsible marketing.
14. Coordinate with the UN Inter-Agency Coordination Group (IACG) and the G20 R&D Hub on the access agenda.
15. Facilitate collaboration of national control labs (NCLs) on preparation of reference reagents and standards.
16. Promote human resource development and use of ICT initiatives for process & product development, preparation of reference standards & reagents in labs & regulation of medical products.
17. Explore Public Intellectual Property Resource for Agriculture (PIPRA) model to reset norms in technology transfer and licensing of biomedical innovation from publicly funded research institutions.

18. Develop measures of accountability for fair returns on public financing of biomedical R&D and counting the social returns from such investment.
19. Host a global discussion on the clinical trials framework with a view to support R&D and access initiatives including predictable regulatory pathways for emergencies- focusing on pharmaceuticals, vaccines, devices and diagnostics.

Plenary Session 3: Fostering Local Production, Technology Transfer and Market Entry Barriers for Medical Products

Chair: **Mr Sudhansh Pant**, Joint Secretary, Department of Pharmaceuticals, Ministry of Chemicals and Fertilizers, Government of India

Lead discussants:

1. **Dr Jitender Sharma**, CEO, Andhra Medtech Zone, and Advisor, Kalam Institute of Health Technology, Andhra Pradesh, India- *Integration of Research, Industry Promotion and Service Delivery*
2. **Dr Gaby Vercauteren**, Senior Advisor, Regulatory Systems Strengthening Team, Essential Medicines and Health Products Department, WHO HQ, Geneva- *WHO Model Regulatory Framework for Medical Devices*
3. **Dr Eswara Reddy**, Joint Drugs Controller, Central Drug Standard Control Organization (CDSCO), India- *Regulatory Framework for Medical Devices in India*

Panelists:

1. **Dr Andrew Rintoul**, Scientist, Pricing & Health Technology Assessment, World Health Organization, Geneva- *Developing Countries Collaborative Arrangements to Boost Local Pharmaceutical Manufacturing Capacity*
2. **Dr Diana Tay**, Business Development Manager, Wellcome Trust, UK- *Funding R&D through Portfolio Development for Health Care Innovations*
3. **Ms Deepanwita Chattopadhyay**, Chairman & CEO, Innovation Knowledge Park, India- *Nurturing Innovative Companies and Developing a Sustainable Innovation Cluster*
4. **Dr Eur Ing Muthu Singaram**, CEO, Healthcare Technology Innovation Centre, Indian Institute of Technology Madras, India- *Addressing Diverse Parameters on Medical Devices Operability for Public Health Needs*

The objective of the session was to examine how to facilitate local production and technology transfer and address collaborative arrangements to enable access to medical products.

The topics addressed "**Fostering Local Production, Technology Transfer and Market Entry Barriers for Medical Products**"

1. WHO model regulatory framework for Medical devices
2. Regulatory framework for medical devices in India
3. Developing and establishing high end technologies
4. Developing countries collaborative arrangements to boost local pharmaceutical manufacturing capacity
5. Nurturing innovative companies and developing a sustainable innovation cluster
6. Addressing diverse parameters on medical devices operability for public health needs

Recommendations:

Recommendations for National Governments

1. Develop sustainable innovation clusters bringing together academic and R&D institutions,

industry, innovators, innovation support systems like incubators, funding agencies – grants, venture capital, regulatory professionals, intellectual property professionals, vendors, contract research organizations (CROs), pilot scale manufacturing facilities and supply chain mechanisms.

2. Develop India as a hub for affordable medical devices as has been the contribution of the country in the pharmaceutical and vaccines sectors.
3. Focus research on critical components pertaining to medical devices by supporting institutions involved in R&D, industry and knowledge repositories.
4. Encourage diffusion of knowledge and sharing of regulatory information, through common facilities for API, medical device parks, innovation clusters.
5. Revitalize the bulk drug segment in India by focus on the Small and medium enterprises (SME) sector to meet national and global public health needs.

Recommendations for WHO/ International Organizations

1. Strengthen National Regulatory Authorities (NRAs) and provide technical support for capacity building for all medical products including medical devices and diagnostics.
2. Facilitate access to safe, appropriate and affordable quality *in-vitro* diagnostics in an equitable manner and suitable for use in resource-limited settings.
3. UNITAID to collaborate and support WHO for R&D, access, regulatory capacity building for quality *in-vitro* diagnostics in countries including technical support for prequalification for IVDs.

Parallel Session 3: Infectious Disease Control: What are the Pathways to Technology Development and Access to Medical Products?

***Chair:* Dr VK Paul**, Member, NITI Aayog, GOI

***Co-chair:* Dr RK Vats**, Additional Secretary, Ministry of Health and Family Welfare, GOI

Lead discussants:

1. **Dr Stephen B Kennedy**, Coordinator for EVD Research, Incident Management System, Ministry of Health, Liberia- *Country Perspectives on R&D in Infectious Diseases including the Ebola Epidemic*
2. **Dr Gagandeep Kang**, Executive Director, Translational Health Science and Technology Institute, India- *Building strong Inter-Disciplinary Research Teams for Technology Development and access to Quality Health Products*

Panelists:

1. **Ms Sunita K Sreedharan**, Lawyer, SKS Law Associates, India- *Intellectual Property Management for Technology Development and Access to Medical Products*
2. **Ms Michelle Childs**, Head of Policy and Advocacy, Drugs for Neglected Diseases (DNDi), Latin America- *Implementing Internationally agreed R&D Principles for Innovation and Access including for AMR*
3. **Mr Damiano De Felice**, Director of Strategy, Access to Medicines Foundation, Netherlands- *Challenges of Access to Medicine Worldwide: The Access to Medicine Index*
4. **Dr Pramod Garg**, Professor, Department of Gastro Enterology, All India Institute of Medical Sciences, India- *Clinician's Perspective on Technology for Infectious Disease Control*
5. **Mr Christoph Spennemann**, Legal Officer and Officer-in-Charge, Intellectual Property Unit, United Nations Conference on Trade and Development, Geneva- *Current Challenges for Investing in R&D in Antibiotics*
6. **Dr Kamal Jayasinghe**, Director General, Chief Executive Officer, National Medicines

Regulatory Authority, Sri Lanka- *Regulatory support for Local Production, Technology Transfer and Market Entry Barriers for Medical Products*

The objective of the session was to discuss R&D initiatives for development of vaccines for infections of epidemic potential and WHO's leadership in Global Antibiotic Partnership for infectious disease control. R&D Blueprint which can be effectively used to address the issue of epidemics and improve R&D preparedness and response, focusing on a list of priority diseases in line with recommendations from a number of expert panels and commissions.

The following topics were discussed:

1. Country perspectives on R&D in infectious diseases including the Ebola epidemic
2. Building strong inter-disciplinary research teams for technology development and access to quality health products
3. Intellectual property management for technology development and access to medical products
4. Implementing internationally agreed R&D Principles for innovation and access including for AMR
5. The World Health Organization and pandemic protection in a globalized world
6. Challenges of access to medicine worldwide: the Access to Medicine Index
7. Clinician's perspective on technology for infectious disease control
8. Current challenges for investing in R&D in antibiotics

Recommendations:

Recommendations for National Governments

1. Provide impetus to TB research consortium activities identified for next five years relating to new drugs, shorter drug regimens and cost effective indigenous diagnostic tools.
2. Facilitate implementation processes for clinical trials, licensing of products and mass immunization of innovative vaccines to counter epidemics.
3. Develop national observatories and/ or coordinate with the global observatory envisaged in the GSPA.
4. Provide for private sector companies to have a publicly available policy on their contribution to improving access to health technologies setting out general and specific objectives, timeframes, reporting procedures, lines of accountability and a governance system that includes direct board-level responsibility and accountability.
5. Monitor hospital acquired infections and antibiotics resistance through intensive care unit (ICUs) rating and mandatory hospital audits.

Recommendations for WHO/International Organizations

1. WHO Global Health Observatory to provide analyses of gaps in health R&D in all areas of public health importance to guide priority-setting, develop and support national and global systems.
2. WHO Expert Committee, follow on from the Advisory Committee on Health Research for health R&D, to initiate calls for proposals by analyzing product profiles and the existing pipeline of products and technologies.
3. Provide technical support for risk-benefit analysis, toxicity study, Pharmacokinetic / pharmacodynamic interactions on fixed dose combinations (FDCs) which have been recommended for concomitant administration.
4. Explore feasibility of inclusion of neglected diseases for facilitating fast track regulatory approval pathway, such as in HIV and HCV etc. for combination products.

Parallel Session 4: Alternative Models of R&D-Industry-Academia Collaborations

Chair: **Mr Ed Whiting,** Director of Policy and Chief of Staff, Wellcome Trust UK

Lead discussants:

1. **Dr Renu Swarup**, Department of Biotechnology, BIRAC, Government of India, *Biotechnology – Next Frontier for Medical Products- National Ecosystem and Bio-Incubators*
2. **Dr Madhu Dikshit**, Director, Central Drug Research Institute (CDRI), India- *CDRI Experience in Drug Discovery Research in India*
3. **Dr YK Gupta**, Professor and Head Department of Pharmacology, All India Institute of Medical Sciences, India- *Implementing Government Commitments to Provide Quality Medicine at Affordable Prices: Challenges before National Essential Medicine Committees*

Panelists:

1. **Dr Mohga Kamal Yanni**, Senior Health and HIV Policy Adviser, Oxfam GB, UK- *International Agencies Support for Models of R&D-Industry-Academia Collaborations*
2. **Ms Siti Aida Abdullah**, Deputy Director, National Pharmaceutical Regulatory Agency, Ministry of Health, Malaysia- *Clinical Trials - the Malaysian Experience*
3. **Dr Viviana Munoz Tellez**, Coordinator, South Centre, Switzerland- *Promoting Innovation in new Antimicrobial Medicines, Vaccines, and Diagnostics*
4. **Professor Margo A Bagley**, Asa Griggs Candler Professor of Law, Emory University School of Law & Senior Fellow, Centre for International Governance Innovation, Atlanta- *Innovative Approaches for Research on Neglected Diseases: The Emory Experience*

The objective of the session was to discuss the industry- academia collaboration to promote R&D of medical products.

The following topics were discussed:

1. Biotechnology – next frontier for medical products- national ecosystem and bio incubators
2. CDRI experience in Drug discovery research in India
3. Implementing Government commitments to provide quality medicine at affordable prices: challenges before National Essential Medicine Committees
4. International agencies support for Models of R&D-Industry- Academia Collaborations
5. OECD perspectives on Models of R&D Industry-Academia Collaborations
6. Promoting Innovation in New Antimicrobial Medicines, Vaccines, and Diagnostics
7. Developing novel therapeutic proteins targeting infectious diseases
8. Innovative approaches for research on neglected diseases: the Emory experience

Recommendations:

Recommendations for National Governments

1. Explore to create separate entities with universities to engage people experienced in the drug development process with focus on technology in areas of expertise including for mixed portfolio of projects (in major market and neglected diseases).
2. Consider the establishment of public private partnership models in the area of Clinical Research Organizations (CROs) to provide speedy and reliable clinical research support for quality studies to encourage medical professionals to conduct clinical trials.
3. Consider partnership with industry to support high risk, transformational technology/process development on a cost sharing basis.
4. Prioritize and increase sustainable public financing for R&D that addresses key un-meet health needs for emerging infectious and non-communicable diseases.

5. Fund incentive mechanisms that de-link the financing of research from sales and prices of health technologies.
6. Induct medical and pharmacy colleges into drug development and R&D including for clinical trials
7. Focus on development of inter- disciplinary skills for product innovation.
8. Build an environment for accelerating translational research by promoting industry-academia collaboration.

Recommendations for WHO/International Organizations

1. Strengthen institutional capacities for Good Laboratory Practices (GLP) for safety pharmacology studies & acute toxicity studies
2. Develop fit for purpose access models – (countries that can do the innovation to be linked with countries who need the innovations through mechanisms such as e- platforms).

Parallel Session 5: Achieving SDGs: Use of Information and Communications Technology (ICT) Initiatives including in Trade Agreements

Chair: **Dr Sanjay Mehendale**, Additional Director General ICMR, Government of India

Co-chair: **Dr GN Singh**, Drugs Controller General (India)

Lead discussants:

1. **Dr VG Somani**, Joint Drugs Controller, Central Drugs Standard Control Organization, India- *E-Governance Initiative at Central and State Level National Regulatory Authorities*
2. **Dr Ananda Sen Gupta**, CEO & Founder, Trackmybeat Health Care Private Limited, India- *Innovative Health Technologies and Health Care Management*

Panelists:

1. **Professor Brook K Baker**, Professor of Law, North Eastern University, USA- *Negotiating for Better Access to Promote Early Market Entry of Medical Products*
2. **Professor Suptendra Nath Sarbadhakari**, Project Director, National Health Portal, India- *Improve Access to Services through IT Enabled Tools: National Health Portal in India*
3. **Dr Vinay Goyal**, Professor, Department of Neurology, Neurosciences Centre, All India Institute of Medical Sciences, India- *Clinical Perspectives on ICT Tools in Health Care*

The objective of the session was to discuss the use of ICT tools for better health care innovation and management. The National Health Portals role in dissemination of information is critical. Policies which could be implemented by the national governments to provide e-healthcare information to ensure transparency and greater accessibility for healthcare management were covered.

The following topics were discussed:

1. Innovative health technologies and health care management
2. Collaborating for medical technology development: the India- Stanford biodesign experience
3. E- governance initiative at Central and State level National Regulatory Authorities
4. Negotiating for better access to promote early market entry of medical products
5. Improve access to services through IT enabled tools: National health portal in India
6. Clinical perspectives on ICT tools in health care

Recommendations:

Recommendations for National Governments

1. Foster e-governance initiatives in regulatory authorities for ease of business, real time status of applications, instant communication and efficient workflow with auto generated legal forms, data analysis and digital archival of records
2. Develop rules & regulations that are unambiguous and may be used countrywide with equally acceptable for e-Prescriptions, mobile Health (m-Health) applications, Telemedicine, including tele-homecare applications.
3. Harmonize different Standards like EHR (Electronic Health Record) Standards, M2M (Machine to Machine) Standards and all other related Standards for achieving optimal outcomes.
4. Ensure quality control for safe online pharmacy applications
5. Develop domain experts (Health Informaticians) in regulatory system for e-Health / Digital Health
6. Create database of retail and wholesale licenses in the country through ICT tools.

Recommendations for WHO/International Organizations

1. Drive local evidence based research on, and, with usage of ICT, and promote understanding for long term value of collecting large volume of Patient data, and population data analytics
2. Build relevant capacity for health informatics professionals for all countries.
3. Encourage creation of local and global health and service delivery protocols.

Plenary Session 4: TRIPS, UN High Level Panel Report and Benefit sharing for access to medical products

Chair: **Mr Anadee Nath Misshra**, Additional Secretary (OSD), Ministry of Law and Justice, Government of India

Co-chair: **Justice Ravindra Bhat**, Judge, High Court of Delhi, India

Lead discussants:

1. **Dr Biswajit Dhar**, Professor, Jawaharlal Nehru University, India- *Role of Publically Funded Universities, Research Institutions, Patenting and Licensing Practices for Prioritizing Public Health*
2. **Professor SK Verma**, Secretary General, Indian Society of International Law, India- *Implementation of TRIPS Provisions and UN HLP Recommendations to Strengthen IP Laws for Ensuring Global Access to Medical Products and health technologies*

Panelists:

1. **Professor Brook Baker**, Professor of Law, Northeastern University, USA- *Public Health in Bilateral Investment Treaties*
2. **Dr Olasupo Owoeye**, Senior Lecturer, Law, RMIT Graduate School of Business and Law, Australia- *Role of PDPs for Access to Health Technologies and Affordable Medical Products*
3. **Dr Carlos Correa**, Special Advisor, South Centre, Switzerland- *Access, Benefit Sharing and New Models to Encourage R&D for Medical Products*
4. **Dr Greg Perry**, Executive Director, Medicines Patent Pool, Switzerland- *Innovative Mechanisms and Voluntary Licensing (Including MPP): Access to Medical Products*
5. **Dr Tjandra Yoga Aditama**, Senior Advisor, World Health Organization-South East Asia Regional Office, India- *Pandemic Influenza Preparedness (PIP) Framework, Access and Benefit Sharing*
6. **Mr Shiba Phurailatpam**, Director of the Asia Pacific Network of People Living with HIV

(APN+), Thailand- *UN HLP Report: Ensuring Access for All*

The objective of the session was to discuss the TRIPS Agreement and the impact on access to medicines in the context of the SDG goals. This Session also focused on PDPs (Product Development Partnerships) which is a novel method of product development wherein a non-profit organizational structure enables the public, private, academic, and philanthropic sectors to aggregate for access to medical products.

The topics addressed in **"TRIPS, UN High Level Panel Report and Benefit sharing for access to medical products"** are:
1. IP issues in medical products including trademarks and patents in TRIPS Agreement
2. Role of publically funded universities, research institutions, patenting and licensing practices for prioritizing public health
3. Implementation of TRIPS provisions and UN HLP recommendations to strengthen IP laws for ensuring global access to medical products and health technologies
4. Public health in Bilateral Investment Treaties
5. Role of PDPs for access to health technologies and affordable medical products
6. Access, benefit sharing and new models to encourage R&D for medical products
7. Innovative mechanisms and voluntary licensing (including Medicine Patent Pool): Access to Medical products

Recommendations:

Recommendations for National Governments
1. Develop negotiation platforms with qualified mediators for voluntary licenses with industry for access at affordable costs.
2. Use compulsory license for access and reduce the cost of medical products in line with TRIPS agreement of WTO.
3. Set up an advisory body in legal institution, such as Indian Society of International Law (ISIL), to provide technical inputs and legal support for health products for achieving the SDG 2030 agenda across all the ministries.
4. Set up appropriate mechanisms to reduce the time to reach clinical proof of concept in medicine development for cancer, immunological, respiratory, neurological and neurodegenerative diseases.

Recommendations for WHO/ International Organizations
1. Explore benefit sharing partnership models such as the Pandemic Influenza Preparedness or PIP framework for anti-virals and vaccines based on assessment of public health risk and need.
2. Conduct detail review of the WHO's work on TRIPS flexibilities for access to medical products for the past five years.
3. Create an online repository for PDPs and develop systems for tracking progress on PDPs in medical products space.
4. Create a legal framework for voluntary license agreements and facilitate negotiation with companies for access at affordable costs.
5. Develop diagnostic and treatment biomarkers for priority diseases taking into account clinical relevance, and approval by regulators to increase the success rate in clinical trials of priority medicines.
6. Develop regional strategy for using PDPs including for LDCs and African countries.

Parallel Session 6: Patents, Intellectual Property, Price Control and Competition Law in Access to Medicines

***Chair:* Mr Anadee Nath Misshra**, Additional Secretary (OSD), Ministry of Law and Justice, Government of India

***Co-chair:* Mr GR Raghavender**, Joint Secretary, National Mission for Justice Delivery and Legal Reforms, Ministry of Law and Justice, GOI

Lead discussants:

1. **Dr Luca Arnaudo**, Senior officer at the Italian Competition Authority, Rome- *Role of Competition authority for adequate and affordable supply of medical products*
2. **Dr Peter Beyer**, Senior Advisor, Department Of Essential Medicines and Health Products, World Health Organization, Geneva- *New Global initiatives in access to medical products: Global Antibiotic Research and Development Partnership (GARDP)*

Panelists:

1. **Professor Stephen Sammut**, Senior Advisor ABLE and Biotechnology Industry Organization, USA- *Health Technology and Entrepreneurial Education Models for the Emerging Markets*
2. **Mr Christoph Spennemann**, Legal Officer and Officer-in-Charge, Intellectual Property Unit, United Nations Conference on Trade and Development, Geneva- *Role of International Agencies including UNCTAD in Facilitating Public-Private Cooperation for access to medical products*
3. **Professor Christoph Rademacher**, Associate Professor, Waseda University, School of Law, Japan- *Protecting and stimulating pharmaceutical innovation – a short review of the Japanese Experience*
4. **Ms Judit Rius Sanjuan**, Consultant, United Nations Development Program, USA- *New Models of Innovation: Practices in Various Countries*

The objective of the session was to discuss the role of Patents, Intellectual Property, and Price Control through Competition Law for Access to Medical products.

The following topics were discussed:

1. Patentability Criteria in national laws for medical technologies and biologicals
2. Role of competition authority for adequate and affordable supply of medical products
3. New global initiatives in access to medical products: Global Antibiotic Research and Development Partnership
4. Role of international agencies including UNCTAD in facilitating public-private cooperation for access to medical products
5. Patent Enforcement in Japan
6. Price Control Mechanisms for access to medical products: perspectives on practices in various countries

Recommendations:

Recommendations for National Governments

1. Engage proactively for safeguarding public health in international trade aspects that are becoming increasingly important such as intellectual property, government procurement, competition laws, environment, etc.
2. Develop tracking mechanisms for pay-for-delay agreements in medical products by collaborating with competition commissions/ antitrust bodies.

3. Governments should be encouraged to raise the issues of undue pressure on their policies during the Trade Policy Review Mechanism ("TPRM") of WTO.

Recommendations for WHO/International Organizations

1. WTO should revisit and examine the 2003 Para 6 system of the Doha declaration to make it workable.
2. Engage in capacity building at national and international levels for public health, including capacity building of patent examiners by the trilateral cooperation forum of international agencies, WHO, WIPO and WTO.
3. Engage on technical content development on trade and intellectual property rights for access to medical products taking into account declarations such as Max Planck institute 'Declaration on Patent Protection – Regulatory Sovereignty'.
4. Engage with international organizations such as UNDP to explore new public & private collaborative models for technology transfer for public health, learning from NIH engagements, Bayh Dole Act & relevant public & private engagements in other jurisdictions.
5. Collaborate with UN organizations such as UNCTAD to facilitate public-private cooperation on public health, develop a framework for health and medical products.
6. Leverage the implementation of GARDP framework for R&D stewardship and access to medical products.

Parallel Session 7: WTO Trade Agreements influencing Health Products– Context SDGs

Chair:

1. **Mr Sudhanshu Pandey**, Joint Secretary- Trade Policy Division, Ministry of Commerce and Industry, Government of India
2. **Mr Sudhansh Pant**, Joint Secretary, Department of Pharmaceuticals, Ministry of Chemicals and Fertilizers, Government of India

Lead discussants:

1. **Dr Sachin Chaturvedi**, Director General, Research & Information System for Developing Countries (RIS), New Delhi, India
2. **Dr Manisha Shridhar**, Regional Advisor, World Health Organization- South East Asia Regional Office, India- *Interpreting public health provisions in trade agreements for achieving SDG Goals*

Panelists:

1. **Dr Gregory Messenger**, Lecturer in Law, School of Law and Social Justice, University of Liverpool, UK- *Sustainable Development Goals, subsidies and trade*
2. **Dr Reji K Joseph**, Associate Professor, , Institute for Studies in Industrial Development, India- *Measures to reduce import dependence on bulk drugs*
3. **Dr VG Hegde**, Professor, Centre for International Legal Studies, School of International Studies, Jawaharlal Nehru University, New Delhi- *UNICTRAL's contribution to the development of trade and health law*

The objective of the session was to analyse various options to facilitate the national policy on the issues of trade and health interface for purposes of nutrition, labelling, packaging and information on foods according to international standards such as Codex Alimentarius for public health goals in the framework of TBT and SPS Agreements. The session explored preventive measures in trade that are necessary for public health in the wake of increasing incidence of communicable diseases (CDs) and non-communicable diseases (NCDs) across all countries.

The following topics were discussed:

1. Interpreting public health provisions in trade agreements for achieving SDG Goals
2. Policy coherence between trade and health policies with reference to Agreement on the Application of Sanitary and Phytosanitary Measures (SPS) and Technical Barriers to Trade Agreement (TBT) of WTO.
3. Emerging Challenges in genetically modified (GM) technologies for public health

Recommendations:

Recommendations for National Governments

1. Develop expertise to negotiate and interpret public health provisions in WTO, Free Trade Agreements (FTAs) and international investment agreements.
2. Focus attention to direct and indirect public health impact of trade interface in the SDG goals for long term sustained gains.

Recommendations for WHO/International Organizations

1. Engage with UNCITRAL (predating WTO agreements such as TRIPS, SPS, TBT), a core legal body of the United Nations system in the field of international trade law in the context of growing burden of CDs and NCDs, for forward looking legal engagement on trade and health interface for the 2030 SDG agenda.
2. Engage in rule making, such as for food labelling, in TBT agreement of WTO for appropriate balance in the health and trade interface.
3. Explore the impact of related WTO agreements such as the Agreement on Subsidies and Countervailing Measures (ASCM) for healthy food choices and tackle subsidies in certain potentially harmful foods.
4. Assist Member countries in consultative mechanisms with legal, finance, public health expertise at national and international levels.

Parallel Session 8: Achieving SDGs: Regional Agreements, Challenges (TRIPS plus Agreements) and Access to Medical Products

***Chair:* Mr Rajiv Aggarwal**, Joint Secretary, Department of Industrial Policy and Promotion, Ministry of Commerce and Industry, GOI

***Co-chair:* Professor SK Verma**, Secretary General, Indian Society of International Law, India

Lead discussants:

1. **Professor TC James**, Consultant, Research and Information System for Developing Countries (RIS), and President, NIPO, India- *TRIPS-Plus Provisions in Trade and Investment Agreements: Advocating for Public Health*
2. **Dr Olasupo Owoeye**, Senior Lecturer, Law, RMIT Graduate School of Business and Law, Australia- *Building Regional Trade Blocs Reflective of the Needs of Developing Countries for Public Health Objectives*

Panelists:

1. **Professor Anthony D So**, MD, MPA, Professor of the Practice and Director, IDEA (Innovation+Design Enabling Access) Initiative, Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA- *Making Intellectual Property Work for Global Health*
2. **Ms Michelle Childs**, Head of Policy and Advocacy, Drugs for Neglected Diseases (DNDi),

Latin America- *Negotiating Licenses in R&D for Patented Compound Libraries and Data*

3. **Dr Burcu Kilic**, Legal Counsel, Public Citizen, USA- *IP Policy, Trade Agreements and TRIPS-plus Rules and Safeguards*
4. **Ms Kajal Bhardwaj**, Consultant, Access to Drugs and Intellectual Property- *Free Trade Agreements after WTO: Public Health Concerns*
5. **Professor Rujitha Shenoy**, Inter-University for IPR Studies, India- *Access to Biomedical Technologies: Biomedical Patents and Sustainable Development Goals*

The objective of the Session was to discuss the challenges to the States in fulfilling their public health obligations in new free trade agreements and explore cooperation for public health goals.

The following topics were discussed:

1. Global governance for public health
2. TRIPS-Plus provisions in trade and investment agreements: advocating for public health
3. Building regional trade blocs reflective of the needs of developing countries for public health objectives
4. Making Intellectual Property work for Global Health
5. Negotiating Licenses in R&D for patented compound libraries and data
6. Free trade Agreements after WTO: Public health concerns
7. Access to biomedical technologies: Biomedical patents and SDGs
8. South-South cooperation for global health and SDGs

Recommendations:

Recommendations for National Governments

1. Balance the aspirations for trade with access to medical products (medicines, vaccines, medical technologies, and diagnostics) to achieve the Sustainable Development Goals.
2. Make a critical appraisal of public health impact, keeping in view the SDG 2030 aspirations, during any negotiations on bilateral, regional and multilateral agreements (FTAs, RTAs) and in existing agreements.
3. Examine and address public health implications in trade agreements such as bilateral investment treaties (BITS) and investor-state dispute settlement (ISDS) on a continuous basis.

Recommendations for WHO/International Organizations

1. Promote availability of intellectual property as non –exclusive licenses and develop public patent pools with public funded research.
2. Take necessary steps towards the adoption of an R&D Convention
3. Address the costs of new molecules/ biologicals in clinical trials where monetary incentives are not available for R&D in diseases specific to developing countries.

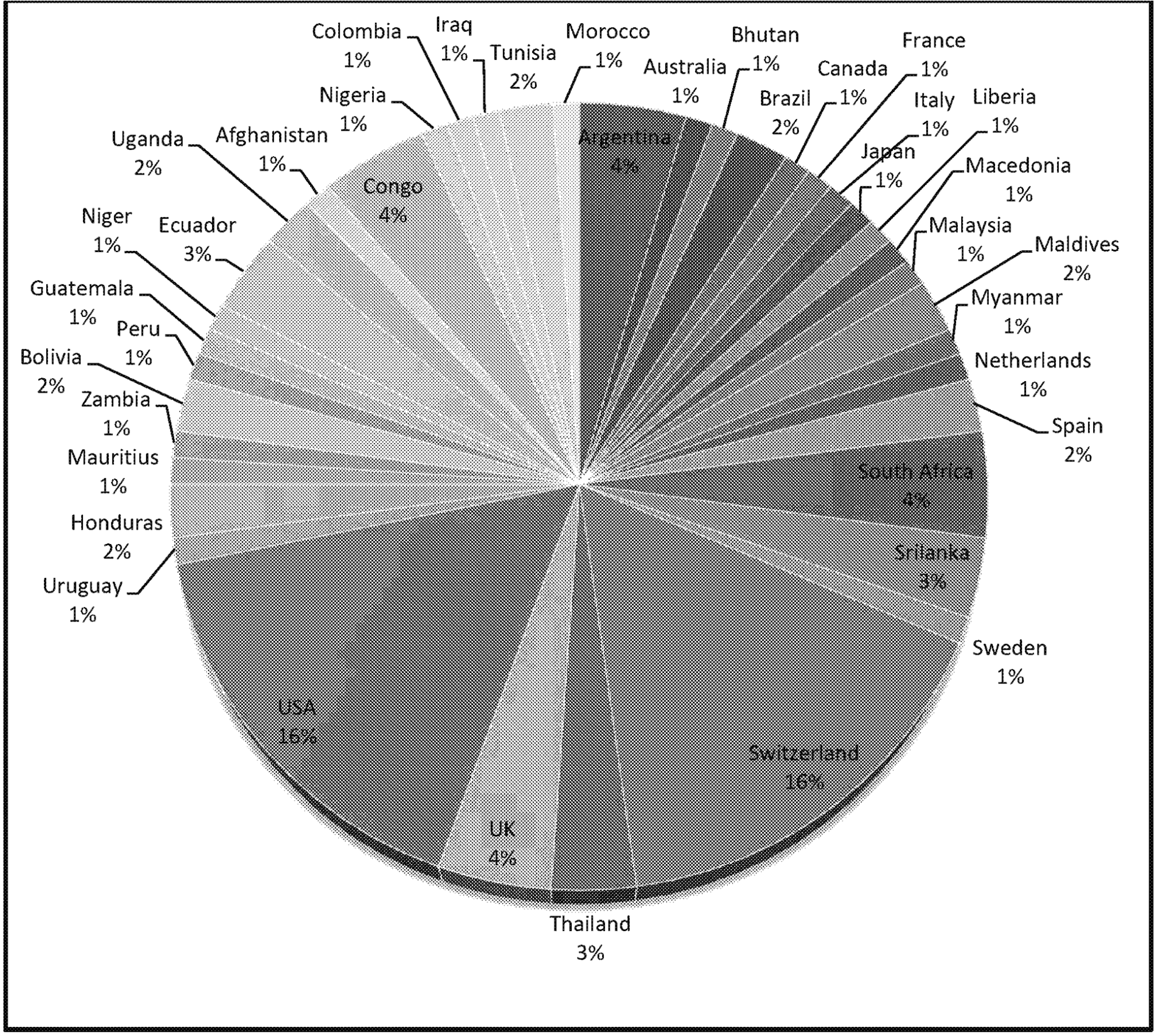
VII. Participants in the Conference

The Ministry of Health, Government of India sought participation from experts from all over the world to deliberate on access to medical products for promoting innovation to attain 2030 Agenda for Sustainable Development. During the side event in WHA 2017, India mentioned that WHO should take the opportunity to engage with all stakeholders to address both innovation and access including rising prices of new pharmaceuticals and rapidly changing requirements for health technologies.

Approximately 285 experts and participants attended, coming from 40 countries including India and from many intergovernmental organizations. There were 191 national and 94 International participants. The distribution of the international participants is given in Figure 1. The attendees came from all six WHO regions. The countries which participated other than India were Argentina, Australia, Bhutan, Brazil, Canada, France, Italy, Japan, Liberia, Macedonia, Malaysia, Maldives, Myanmar, Netherlands, Spain, South Africa, Sri Lanka, Sweden, Switzerland, Thailand, United Kingdom, United States of America, Uruguay, Vietnam, Mauritius, Honduras, Zambia, Bolivia, Peru, Guatemala, Afghanistan, Uganda, Ecuador, Niger, Congo, Morocco, Tunisia, Iraq and Nigeria. Attendees represented a variety of organizations, with the largest numbers from the government or public agencies and academic sectors.

The participation was also from high-level delegates representing United Nations High Level Panel on Access to Medicines, United Nations (UN) organizations, Ministries of Health, Commerce, Foreign Affairs, partner agencies, academia, SAARC & WHO South-East Asia Region countries, civil society organizations and private sector including pharmaceutical and medical device associations.

Figure 1: Country wise distribution of International Participants



Dignitaries in the Conference, Chairs, Co-chairs, Lead Discussants and Panelists

1. HE Mr JP Nadda, Union Minister, Health & Family Welfare, Government of India
2. HE Mr Ashwini Kumar Chaubey, Hon'ble Minister of State, Health & Family Welfare, Government of India
3. HE Ms Anupriya Patel, Hon'ble Minister of State, Health & Family Welfare, Government of India
4. Dr VK Paul, Member, NITI Aayog, Government of India;
5. Ms Preeti Sudan, Secretary, Health, Ministry of Health and Family Welfare, Government of India;
6. Dr Soumya Swaminathan, Secretary, Department of Health and Research & Director General, Indian Council of Medical Research, Government of India
7. Justice Ravindra Bhat, Judge, High Court of Delhi, India
8. Ambassador Dr Virander Paul, Deputy Permanent Representative of India to the United Nations
9. Dr Jagdish Prasad, Director General Health Services, Government of India
10. Dr EMS Natchiappan, President, Indian Society of International Law, India
11. Dr RK Vats, Additional Secretary, Ministry of Health and Family Welfare, GOI
12. Mr Anadee Nath Misshra, Additional Secretary (OSD), Ministry of Law and Justice, Government of India
13. Mr Sudhir Kumar, Joint Secretary, Ministry of Health and Family Welfare, Government of India
14. Mr Lav Agarwal, Joint Secretary, Ministry of Health and Family Welfare, GOI
15. Mr Sudhansh Pant, Joint Secretary, Department of Pharmaceuticals, Ministry of Chemicals and Fertilizers, Government of India
16. Mr GR Raghavender, Joint Secretary, National Mission for Justice Delivery and Legal Reforms, Ministry of Law and Justice, GOI
17. Mr Sudhanshu Pandey, Joint Secretary- Trade Policy Division, Ministry of Commerce and Industry, Government of India;
18. Mr Rajiv Aggarwal, Joint Secretary, Department of Industrial Policy and Promotion, Ministry of Commerce and Industry, GOI
19. Ms Aradhana Johri, Former Secretary Department of Pharmaceuticals (DoP), Ministry of Chemicals and Fertilizers, Secretary of Finance (Disinvestment); Former Additional Secretary, Ministry of Health & Family Welfare, GOI
20. Dr GN Singh, Drugs Controller General (India), Central Drugs Standard Control Organization, India
21. Dr Henk Bekedam, WHO Representative to India
22. Dr Manisha Shridhar, Regional Advisor, Intellectual Property Rights and Trade and Health, WHO SEARO
23. Dr Madhur Gupta, Technical Officer-Pharmaceuticals, WHO Country Office for India
24. Dr SK Verma, Secretary General, Indian Society of International Law
25. Ms Ruth Dreifuss, Co-chair, UN High Level Panel on Access to Medicines; Former President, Swiss Confederation, Geneva
26. Dr Jorge Bermudez, Senior Researcher in Public Health, National School of Public Health, Fiocruz, Ministry of Health, Brazil
27. Dr Mandeep Dhaliwal, Director-HIV, Health and Development Group, United Nations Development Program, USA

28. Dr Peter Beyer, Senior Advisor, Department Of Essential Medicines and Health Products, World Health Organization, Geneva
29. Ms Maria Lorena Di Giano, Executive Director, Fundacio Grupo Efecto Positivo and General Coordinator of RedLam, Argentina
30. Professor Anthony D So, Professor of the Practice and Director, IDEA (Innovation+Design Enabling Access) Initiative, Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA
31. Dr Mohga Kamal Yanni, Senior Health and HIV Policy Adviser, Oxfam GB, UK
32. Mr Anand Grover, Former UN Special Rapporteur and Member- Expert Advisory Group, UN High Level Panel on Access to Medicines, India
33. Dr Renu Swarup, Senior Adviser, Department of Biotechnology and Managing Director, Biotechnology Industry Research Assistance Council- Biopharma Mission, India
34. Dr Gagandeep Kang, Executive Director, Translational Health Science and Technology, India
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36. Dr Anban Pillay, Director, National Department of Health, South Africa
37. Dr Anil Koul, Director, CSIR-Institute of Microbial Technology, India
38. Ms Leena Menghaney, Head- South Asia, Access Campaign, Medecins Sans Frontieres, India
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57. Ms Sunita K Sreedharan, Lawyer, SKS Law Associates, India
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59. Dr Pramod Garg, Professor, Department of Gastro Enterology, All India Institute of Medical Sciences, India
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66. Dr Viviana Munoz Tellez, Coordinator, South Centre, Switzerland;
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Attachments: Pricing of Cancer Medicines and its impacts.pdf

Dear colleagues-

Last night, WHO released a much-anticipated technical report on "Pricing of cancer medicines and its impacts". This report was requested by the 70th World Health Assembly in 2017, (http://apps.who.int/gb/ebwha/pdf_files/WHA70/A70_R12-en.pdf?ua=1) and it will be discussed at the end of January at the WHO Executive Board under the same agenda item as the Roadmap on Access to Medicines. We expect that other Member States will be very interested in the report's findings.

OGA is still reviewing the technical report and will be preparing a position paper on it, which we expect to circulate for your review in January. However, we would also welcome feedback from HHS subject matter experts in the meantime—which hopefully will make the review process a bit easier after the New Year. Please send us any initial feedback you have by **COB on December 31st** to ensure that we are able to take it into account when drafting the position paper.

As always, please let me know if you have any questions.

Best,

Anne Snyder, J.D.
Global Health Officer, Trade and Health
Office of Global Affairs
U.S. Department of Health and Human Services
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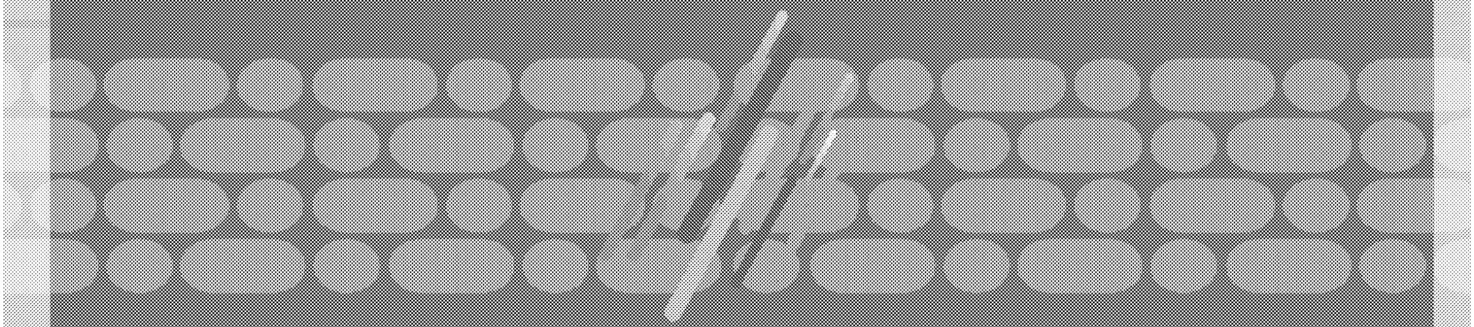
Organization



ACCESS TO MEDICINES, VACCINES AND PHARMACEUTICALS

TECHNICAL REPORT

Pricing of cancer medicines and its impacts

A comprehensive technical report for the World Health Assembly Resolution 70.12 Operative paragraph 2.9 on pricing approaches and their impacts on availability and affordability of medicines for the prevention and treatment of cancer

TECHNICAL REPORT

Pricing of cancer medicines and its impacts

World Health Organization

Pricing of cancer medicines and its impacts

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Abbreviations

AIFA	Italian Medicines Agency
ASCO	American Society of Clinical Oncology
DALY	disability-adjusted life-year
EMA	European Medicines Agency
EML	WHO Model List of Essential Medicines
EML Working Group	Essential Medicine List Cancer Medicines Working Group
ERP	external reference pricing
ESMO	European Society for Medical Oncology
GDP	gross domestic product
HHI	Herfindahl-Hirschman Index
HPV	human papillomavirus
IARC	The International Agency for Research on Cancer
ICR	Institute of Cancer Research
Informal Advisory Group	Informal Advisory Group on Availability and Affordability of Cancer Medicines
IRP	internal reference pricing
MCBS	Magnitude of Clinical Benefit Scale
MEA	Managed Entry Agreement
NGO	nongovernmental organization
NICE	National Institute for Health and Care Excellence
NIH	National Institutes of Health
OECD	Organisation for Economic Co-operation and Development
OS	overall survival
PBS	Pharmaceutical Benefits Scheme
PFS	Progression-free survival
R&D	research and development
US FDA	United States Food & Drug Administration
VAT	value-added tax
WHO	World Health Organization

Executive summary

Scope

1. This report examines pricing approaches adopted by the pharmaceutical industry and authorities responsible for the pricing of medicines, with a specific focus on medicines for the prevention and treatment of cancer. The report reviews pricing approaches applied throughout the "value chain" (i.e., activities required to bring medicines to patients, from R&D to service delivery), and at different time points of product life cycle from market launch to the entry of clinically substitutable medicines (that is, medicines with similar chemical structure and therapeutic effects, so-called "me too" medicines; and generic and biologically similar medicines).

2. This comprehensive technical report presents evidence relating to the impacts of pricing approaches (or lack thereof) on the price, availability and affordability of cancer medicines. It examines the possible relationship between pricing approaches and (a) R&D of cancer medicines, including incentives for investment in R&D on cancer and in innovation of these measures, as well as possible gaps in undertaking research and development (that is, a possible shortfall in funding or activities in certain areas of cancer research); (b) transparency in price and governance; and (c) benefits and unintended negative consequences that would deviate from the original policy intent. Options that might enhance the affordability and accessibility of cancer medicines are outlined in paragraphs 41 and 42 below.

Context

3. Cancer is one of the greatest global public health challenges. There are many types of cancer, with different causes, manifestations and prognoses. The global cancer burden is estimated to have risen to 18.1 million new cases and 9.6 million deaths in 2018. Cancer has broad societal impacts beyond the negative effects it has on individual health outcomes, including productivity losses for cancer patients and their family caregivers.

4. Over the past decades, governments have worked with stakeholders to implement a spectrum of preventative and therapeutic interventions, from vaccination and screening programmes to surgical, pharmacological, radiological and social interventions for the treatment, rehabilitation and palliation of people with cancer. These collective efforts in diagnosis and treatment have resulted in great improvements in survival rates, which nonetheless continue to vary considerably by type of cancer and geographical region. For example, over 80% of children diagnosed with cancer in high-income countries will be cured of the disease, in contrast to rates as low as 10% among children diagnosed with cancer in low- and middle-income countries, which, despite having almost 80% of the burden as measured by disability-adjusted life years, are estimated to have a less than 5% share of global resources for combating cancer.

5. Data from multiple sources show that the rate of growth of expenditure on cancer medicines greatly exceeds the rate of growth of newly diagnosed cancer cases. Increased use of cancer medicines may be partly responsible for the growing expenditure. However, the growing expenditure may be primarily

due to increases in medicine prices or a shift towards using higher-cost cancer medicines. In addition, the rate of growth of expenditure on cancer medicines exceeds the rate of growth of overall health care expenditure.

6. Existing approaches to managing the prices of cancer medicines have not resulted in outcomes that meet policy and economic objectives. Stakeholders continue to voice their concerns about the lack of adequate access to both new and off-patent essential cancer medicines, with high prices cited as a main contributory factor. Furthermore, overall prices of cancer medicines continue to rise, to the extent of impairing the capacity of health care systems to provide affordable, population-wide access to cancer medicines.

7. Access to cancer medicines is linked to systemic factors such as financial resources, insurance coverage, availability and skill set of the health workforce, health care infrastructure and physical access to health services. Thus, strategies to improve people's access to cancer medicines should be considered holistically across all surgical, pharmacological, radiological and social interventions for the prevention, treatment, rehabilitation and palliation of people with cancer. Such strategies should also be assessed with respect to the entire health care sector, so that the benefits of improving access to cancer medicines are not achieved at the expense of essential health care products and services for other disease areas.

Benefits and risks of newer cancer medicines

8. Pricing of cancer medicines is often discussed alongside a discussion of their benefits, particularly for newer cancer medicines. Cancer medicines that target a particular molecular alteration developed in past decades (targeted therapies) may represent advances in the treatment of cancer. Some targeted therapies have been shown to result in substantial improvements in health outcomes, such as overall survival and quality of life, and have transformed patient care for several cancer types. However, literature indicates that a considerable proportion of targeted therapies approved in the past 15 to 20 years have data only for improvement in surrogate endpoints, such as change in tumour size, without evidence of a benefit in terms of survival or quality of life. For some medicines that have been found to have an impact on survival, the size of the benefit may still be small; the average benefit is 3 months, which may be considered marginal by clinical experts. Furthermore, some medicines may present higher risk of toxicities to patients, with evidence of high rates of deaths related to treatment (toxic deaths) and high chances of patients discontinuing treatment due to intolerance. In assessing the benefits of cancer medicines, it is important to conduct a comprehensive evaluation of all evidence by combining results across clinical trials and appraising the consistency of evidence in its totality. It is also important to identify the potential limitations of evidence obtained in terms of its generalizability to different health care systems.

Industry approaches to price-setting

9. The literature describes four broad determinants of medicine prices from the industry perspective: (a) costs of R&D; (b) costs of production and commercialization; (c) the "value" of medicine; and (d) sufficient returns on R&D.

10. Estimates of R&D costs, including for cancer medicines, are highly variable and not transparent. Reported estimates, after adjustments for the probability of trial failure and opportunity costs, range between US$ 100–150 million and US$ 4–6 billion, but the most commonly accepted estimates are between US$ 200 million and US$ 2.9 billion.

11. "Value-based pricing" has been proposed as a method of pricing new medicines. However, there are many uncertainties associated with estimating value, as a result of different technical approaches to assessment, incomplete evidence, comparison with inefficient practices, and different perceptions of value. This method may lead to unaffordable prices for cancer medicines.

12. To examine returns on R&D investments, an analysis was undertaken to examine the sales incomes from cancer medicines approved by the United States Food and Drug Administration from 1989 to 2017 for the originator companies. For the 99 medicines included in the analysis, the average income return by end-2017 was found to be US$ 14.50 (range: US$ 3.30 to US $55.10) for every US$ 1 of R&D spending, after adjustments for the probability of trial failure and opportunity costs; 33 of those medicines had already qualified as "blockbuster drugs" by having an average annual sales income exceeding US$ 1 billion. Many medicines, particularly biologics, continued to generate high sales incomes for the originator companies after expiry of patents and the end of exclusive marketing rights.

13. Overall, the analysis suggests that the costs of R&D and production may bear little or no relationship to how pharmaceutical companies set prices of cancer medicines. Pharmaceutical companies set prices according to their commercial goals, with a focus on extracting the maximum amount that a buyer is willing to pay for a medicine. This pricing approach often makes cancer medicines unaffordable, preventing the full benefit of the medicines from being realized.

Payer approaches to price-setting

14. Authorities responsible for the pricing of medicines have adopted a range of approaches to set medicine prices, including cancer medicines, such as cost-based pricing, value-based pricing, reference pricing, and pricing through tendering and negotiation. Some authorities have also set a maximum "ceiling" price, while others have agreed to arrangements with manufacturers to enable access to cancer medicines subject to specified conditions, such as discounts or rebates based on volume of sales or payment according to health outcomes. These agreements are known as "managed entry agreements" or "risk-share agreements". The conditions of such arrangements are often agreed on confidential terms between manufacturer and purchaser.

15. Authorities in some countries have routinely monitored medicine prices, with a view to controlling prices throughout the supply chain and at various time points throughout the product life cycle. These strategies include regulating mark-up amounts, reassessing prices when there is a change in market conditions, such as entry of generic and biosimilar products, or when the indications for an individual medicine change.

16. Authorities in some countries have also used other strategies to achieve greater system efficiencies and improve access to cancer medicines that may have an indirect effect on prices, including (a) requiring clinicians to obtain approval from the payer before prescribing or dispensing a select set of high-cost

and highly-specialized cancer medicines; (b) implementing policies to encourage prescribing and substitution of cancer medicines with generic or biologically similar products to increase competition; (c) reduction or exemption of taxes on medicines; and (d) implementing pooled procurement of medicines by combining financial and non-financial resources across various purchasing authorities in order to create greater purchasing power through economies of scale and better negotiation position.

Relationship between inputs throughout the "value chain" and price-setting

17. Overall, there are gaps in data and information regarding the activities and costs required to bring medicines to patients, throughout the value chain from R&D to service delivery. Moreover, the precise relationship between "value chain" inputs and price-setting is not known in many countries, particularly in low- and middle-income countries.

Impacts on price

18. Prices and costs of many cancer medicines are high, in recent decades often reaching tens of thousands of US dollars per patient per year, while comparative analyses show that they exceed the prices and costs of medicines used for treating other diseases.

19. Current pricing policies (or the lack thereof) have led to considerable variability in the prices of cancer medicines within a country and across regions. Evidence from published literature shows that the observed price variability does not seem commensurate with the demand or a given country's purchasing power, while existing procurement practices in some countries may not be very efficient. When prices of cancer medicines are higher than a country's ability to pay, this may impair coverage of essential cancer medicines, causing delay in patient access to medicines and limiting the system's ability to achieve the best possible patient health outcomes. Finally, regional differences in medicine prices within a country may cause inequitable access.

20. Evidence suggests that a lack of effective and consistent policies for managing medicine prices across the supply chain (i.e., taxes and mark-up amounts) over time can result in uncontrolled and highly dispersed prices for the same medicine. Furthermore, inconsistent pricing policies across service delivery settings within a health care system (such as hospitals and outpatient facilities) can result in inefficient cost-shifting activities and inequitable access for patients.

21. Comparative analyses indicate that more pricing regulations may contribute to lower medicine prices and costs. Yet even in countries that have implemented a range of policy measures to manage medicine prices, the prices of newer cancer medicines have continued to grow substantially in recent decades. Thus, more measures may be needed to realign the prices of cancer medicines and expand access to cancer medicines by treating higher patient numbers at lower average costs, thus ensuring the long-term financial sustainability of health care systems and industries.

22. Policies that facilitate price competition among pharmaceutical companies for clinically substitutable medicines have generally led to lower prices of generic brands compared to their originator counterparts, yielding expenditure savings. However, the extent to which pricing policies can enhance competition and reduce medicine prices is dependent on a range of factors, such as existing price and

non-price policies; the number of competing companies and the size of products and markets; regulatory requirements and processes for generic and biosimilar medicines; and enforcement of robust competition policies to prevent companies from engaging in behaviours that may impair competition. Documented examples of anti-competitive behaviours by companies include introduction of "pseudo-generics", tacit or actual collusion, "product hopping" (switching a patented medicine to a modestly reformulated product that offers little or no therapeutic advantages in order to preserve market exclusivity) and wasteful non-value-added activities, such as lobbying or filing patent clusters to delay generic/biosimilar entry.

Impacts on availability

23. Two large surveys examined the availability of medicines for solid tumours in the national formularies of 49 European countries in 2014 and 63 countries outside Europe in 2016. Data showed that countries with lower national income had lower availability of cancer medicines, or availability only with higher out-of-pocket patient payments, especially for higher-cost medicines, including targeted therapies. One survey found that 32.0% and 57.7% of essential medicine list cancer medicines were available in lower-middle-income countries and low-income countries, respectively, only if patients were willing to incur their full costs.

24. Case studies from several countries show that the judicious selection of cancer medicines and the rational application of access requirements with consideration of the specific health-system context can deliver better health outcomes to cancer patients for the available financial resources. A policy of trying to fund the same number of cancer medicines as are available in other countries will not result in substantive health improvements, but will result in significantly higher costs. Countries should instead consider their specific health care context, including factors such as population need and available funds.

25. However, there is evidence that in some countries, cost-containment measures undertaken due to the high costs of cancer medicines, irrespective of population needs, have resulted in reduced, delayed and even cancelled treatment, which may have adverse impacts on patient health outcomes. While differences in system capacities and population needs must be recognized, policies for controlling costs to ensure system sustainability must be balanced with the primary objective of facilitating timely patient access to medicines.

Impacts on affordability

26. A modelling study shows that universal coverage of cancer medicines alone, at 2018 prices, would greatly exceed a generously assumed budget of 5% of the total health care expenditure: standard treatment regimens for a selected set of cancers would cost much more than the estimated annual per-patient "budget" of US$ 800 (low-income countries) to US$ 40 600 (high-income countries).

27. In the absence of insurance coverage, cancer treatment is unaffordable for many patients. A course of standard treatment for early stage HER2 positive breast cancer (doxorubicin, cyclophosphamide, docetaxel, trastuzumab) would cost about 10 years of average annual wages in India and South Africa and 1.7 years in the United States of America. The costs associated with other medical care and

interventions (such as surgical interventions and radiotherapy) and supportive care (such as anti-emetics and haematopoietic growth factors) would make overall care even more unaffordable. Even with insurance coverage, patients living with cancer in many countries have reported financial stress, to the extent that they may lower the treatment dose, partially fill prescriptions or even forego treatment altogether.

Impacts on R&D

28. In 2017, there were almost twice as many registered clinical trials on cancer medicines as in the next four highest therapeutic categories combined. Leading experts have noted significant inefficiencies of cancer drug trials due to duplication of research efforts and the pursuit of marginal therapeutic indications with non-clinically significant health outcomes. Some failed investments could have been prevented given the lack of compelling evidence of efficacy in humans prior to embarking on major clinical trial programmes.

29. While acknowledging the tremendous challenges in finding effective and safe cancer medicines, the trial redundancy (that is, duplication of trials that may be unnecessary) of cancer medicines suggests that excessive financial returns combined with market dominance have encouraged companies to engage in excessive risk-taking in R&D by investigating cancer medicines despite the lower probability of success. Simultaneously, companies have adopted a "de-risking" strategy by pursuing marginal indications with the expectation that the market would continue to bear high prices in the name of so-called "innovation". In the long term, such distortion of investment and corporate behaviour will stifle genuine innovation.

30. Concerns that lower cancer medicine prices might impair future R&D seem misplaced because evidence suggests that (a) prices of cancer medicines bear little or no relationship with R&D costs; (b) financial returns of cancer medicines are high; (c) potential impact on revenue due to lower prices could be offset by higher volume, especially when the marginal cost of production is low; and (d) governments and the non-profit-making sector have made substantial contributions to the R&D of medicines through direct funding and other incentives.

31. The public sector has made a wide range of contributions to the R&D of medicines generally, including cancer medicines, ranging from providing direct funding of basic science research and clinical trials to building physical research infrastructure, supporting the operation of institutions such as cancer registries, building medical research workforces through education programmes and incentivizing R&D through tax credits or reductions. Such public-sector investment has often led directly to the discovery and development of cancer medicines such as abiraterone, temozolomide and enzalutamide.

32. Given this consideration, some stakeholders have questioned whether pharmaceutical companies can legitimately claim to recover the full costs of R&D by setting high prices for medicines. They see a need to clarify whether the public has been "paying twice", or should be paying twice, for medicines developed with at least partial support from public resources. It is also important to clarify the relationship between the government, industry and universities when pursuing joint research ventures.

33. Determining research priorities and gaps requires both technical assessments and value judgments. Studies have suggested that research on haematological and breast cancers may be overfunded, while research on cancers of the liver, thyroid, lung, oesophagus, stomach, bladder and pancreas may be underfunded; these studies have assumed that the allocation of research funding for each type of cancer should be in proportion to their respective disease burden. However, as society may have a higher preference to help children and young mothers, the prioritization of research for haematological and breast cancers may be considered justified.

Impacts on price transparency

34. The use of discounts and rebates may signal competition in the market and is often considered a legitimate competitive practice if applied legally. However, confidential agreements on rebates and discounts have obstructed market transparency, including information about the level of price competition.

35. Growing differences in list prices and net transaction prices of medicines (i.e. after discount and rebates) may mask actual increases in medicine price. Pharmaceutical companies may also be motivated to keep list prices high to impair the effectiveness of external reference pricing.

36. Non-transparent medicine prices may conflict with the principles of good governance and confidential agreements may compromise clear lines of accountability. A lack of price and process transparency may even lead to corruption, especially in health care systems with weak overall governance.

37. Theoretical arguments on whether greater price transparency would lead to higher or lower medicine prices are inconclusive. There is a lack of evidence of the effectiveness of confidential agreements in lowering prices and improving access. On the other hand, there is limited context-specific evidence that improving price transparency has led to better price and expenditure outcomes. Nonetheless, improving price transparency should be encouraged on the grounds of good governance.

Unintended negative consequences

38. Current R&D incentives, regulatory flexibility and pricing practices for medicines to treat rare diseases (orphan drugs) may have led pharmaceutical companies to pursue an indication for rare cancer in the first instance and then expand the indication to other more common cancers, with a view to gaining faster market entry at high prices.

39. There have been documented cases of disruption in the supply of cancer medicines in recent years. Causes of medicine shortages are complex and involve both supply and demand factors. Low market attractiveness due to low prices and small market sizes are possible contributing factors as well. However, data from regulatory reporting indicate that shortages of cancer medicines are probably due to problems related to meeting the quality standards for injections, rather than to lack of financial incentives to ensure the ongoing supply of lower-priced medicines. Overall, existing data on medicine shortages are not robust. Until more compelling evidence is presented, payers should not be deterred from seeking lower prices for fear of causing shortages. This will minimize the incentive for suppliers to prioritize higher-priced and more profitable medicines over lower-priced medicines.

40. There are some documented examples of inefficient, unethical and even illegal activities induced by the high prices or profitability of cancer medicines, including the emergence of substandard or falsified cancer medicines, practices prohibited by antitrust laws, deceptive marketing and activities for off-label prescribing.

Options that might enhance affordability and accessibility

41. A set of options that might enhance the affordability and accessibility of cancer medicines have been identified through a review of policy and evidence and consultations with experts, broadly pertaining to: (a) strengthening pricing policies at the national and regional levels; (b) improving the efficiency of expenditure on cancer medicines; (c) improving the transparency of pricing approaches and prices of cancer medicines; (d) promoting cross-sector and cross-border collaboration for information-sharing, regulation and procurement; (e) managing factors that would influence the demand for cancer medicines; and (f) realignment of incentives for R&D.

42. The options and proposed time frame are summarized in the following table.

Table. Options that might enhance affordability and accessibility of cancer medicines, including time frame

Option	Level of action required				Time frame for action*			Proposed actions taken by:				
	Local	Regional	National	International	Short	Medium	Long	Government^	Payer^	Industry	Health care professional	Patients
(a) Strengthening pricing policies												
(a.1) Improving the consistency of policies across health and other sectors	○	●	●		▭	▭		✱	∗	∗		
(a.2) Designing differential pricing sensitive to health systems' ability to pay			○	●		▭	▭	∗	✱			
(a.3) Enhancing health system ability to review and adjust prices, and to withdraw funding for superseded or less cost-effective medicines if required	○	●	●		▭	▭			✱	∗		
(a.4) Enforcing price caps for cancer medicines, with or without progressive reduction of prices over time		●	●		▭	▭			✱			
(a.5) Creating competition among substitutable cancer medicines		○	●		▭	▭		∗	✱	∗	∗	∗
(b) Improving efficiency												
(b.1) Prioritizing the selection of medicines with high(er) clinical value		●	●	○	▭	▭		∗	✱		✱	
(b.2) Considering the costs of model of care as part of the pricing approach		●	●		▭	▭			✱			
(b.3) Considering managed entry agreements for expenditure control only in specific cases			●		▭			∗	✱			
(b.4) Avoiding the use or establishment of fund earmarked for the provision of cancer medicines			●		▭			✱	∗			

Option	Level of action required				Time frame for action*			Proposed actions taken by:				
	Local	Regional	National	Inter-national	Short	Medium	Long	Government^	Payer^	Industry	Health care professional	Patients
(c) Improving transparency												
(c.1) Disclosing the net transaction prices of cancer medicines to relevant stakeholders			●	○	▭	▭		*	*	✱		
(c.2) Disclosing and controlling prices along the supply chain	○	●	●		▭	▭		✱	✱	*	✱	
(c.3) Reporting the costs of R&D and production, including public sources of funding			○	●		▭	▭	*		✱		
(c.4) Communicating pricing and reimbursement decisions to the public, when appropriate		○	●		▭	▭		*	✱			
(d) Promoting cross-sector & cross-border collaboration												
(d.1) Sharing information on medicine prices and technical assessments			●	○	▭	▭		*	✱			
(d.2) Harmonizing regulatory requirements for biosimilar medicines to ensure safety and quality and to promote competition			●	○		▭	▭	✱		*		
(d.3) Streamlining cross-border regulatory requirements and supply management of medicines in shortage			●	○		▭	▭	✱		*		
(d.4) Pooling subnational, national and regional resources for joint negotiation and procurement		●	●			▭		*	✱	*	*	

Option	Level of action required				Time frame for action*			Proposed actions taken by:				
	Local	Regional	National	International	Short	Medium	Long	Government^	Payer^	Industry	Health care professional	Patients
(d.5) Using voluntary license agreements where possible and applying WTO/TRIPS flexibilities for patented medicines, where appropriate			●			▭	▭	✱				
(e) Managing demand-side factors												
(e.1) Removing financial / non-financial incentives for prescribing cancer medicines of limited clinical value	●	●	●		▭				✱	✱	✱	
(e.2) Restricting promotional activities of cancer medicines to clinicians and the public			●		▭			✱		✱	*	
(e.3) Correcting any misperception of inferior quality of generic or biosimilar medicines		○	●		▭	▭		✱	*	*	✱	*
(e.4) Implementing regulatory measures upon identification of substandard and falsified medicines	●	●	●	●	▭			✱		✱	✱	
(f) Realigning incentives for R&D												
(f.1) Incentivizing research for cancers that affect smaller populations			●	●		▭	▭	✱		✱	✱	
(f.2) Focusing on health service research to improve system efficiencies, rational use of medicines and packages of care		●	●		▭	▭		✱			✱	*

Key: WTO/TRIPS: World Trade Organization Trade-Related Aspects of Intellectual Property Rights.

*Short term: within 1 year; medium term: 1–3 years; long term: more than 3 years.

^ Government and payer may be the same

●: Primary level of action; ○: Complementary level of action.

✱: Primary actor; *: Complementary actors.

1 Introduction

In 2017, the Seventieth World Health Assembly adopted resolution WHA70.12 on *Cancer prevention and control in the context of an integrated approach* (Appendix A). Operative paragraph 2.9 of this resolution requests the Director-General:

> To prepare a comprehensive technical report to the Executive Board at its 144th session that examines pricing approaches, including transparency, and their impact on availability and affordability of medicines for the prevention and treatment of cancer, including any evidence of the benefits or unintended negative consequences, as well as incentives for investment in research and development on cancer and innovation of these measures, as well as the relationship between inputs throughout the value chain and price setting, financing gaps for research and development on cancer, and options that might enhance the affordability and accessibility of these medicines.

This report has been prepared in accordance with this operative paragraph.

1.1 Prevention and treatment of cancer

1.1.1 Cancer: A complex public health and health system challenge

Cancer is one of the greatest public health challenges globally. Cancer has a complex disease profile (*1–3*) and comprises a "constellation" of diseases with vastly different etiologies, manifestations and prognoses (*4*). Worldwide, cancer afflicts millions of people each year (*5,6*). The International Agency for Research on Cancer (IARC) projects that, in 2040, the number of new cancer cases and cancer-related deaths worldwide will grow by approximately 1.6–1.7 fold from 2018 estimates to 29.5 million and 16.4 million, respectively (*7*). Cancer has broad societal impacts beyond the negative effects it has on individuals' health outcomes (*8–10*). These include productivity losses for cancer patients and their family caregivers.

In view of the complexity of cancer and the scale of its consequences, governments have implemented a spectrum of interventions to mitigate the current and future impacts of cancer. These include programmes for eliminating or minimizing population exposure to cancer-related risk factors, such as tobacco smoking and human papillomavirus (HPV). The package of interventions may also include early detection programmes, as well as provision of a suite of surgical, pharmacological, radiological and social interventions for the treatment, rehabilitation and palliation of people with cancer. The overall aim of these measures is to create a system that improves the health outcomes of patients with cancer through equitable and sustainable access to, and quality use of, effective and safe interventions.

In addition, like other policy areas, government measures may include an explicit aim of creating an environment for the private businesses and service providers to compete fairly, while encouraging enterprise, efficiency and innovation. Ideally, a competitive environment would create choices for consumers by encouraging suppliers to offer cancer care with lower prices and of higher quality. For this reason, governments often implement policy in partnership with a range of stakeholders from international organizations, academia and non-profit-making organizations, as well as parties from the for-profit sector. This is to ensure shared goals in improving health outcomes through access to the best available interventions.

Over the past decades, collective efforts from all stakeholders have resulted in great improvement in survival of people diagnosed with cancer (Appendix B) (*11*). While encouraging, survival rates continue to vary considerably by types of cancer and among people living in different regions of the world. For example, over 80% of children diagnosed with cancer in high-income countries[i] would be cured of the disease, in contrast to the poor survival rates of possibly as low as 10% among children diagnosed with cancer living in low- and middle-income countries (*12,13*). Furthermore, there is considerable mismatch in the distribution of resources for addressing the challenge of cancer. For example, despite having almost 80% of the burden as measured by disability-adjusted life-years (DALYs), low- and middle-income countries have less than an estimated 5% share of the global resources for cancer (*14*).

Indeed, the majority of patients living with cancer around the world do not receive any timely cancer care, including pharmacological treatment. In addition, where treatment was provided, the therapy might not have been appropriate or safe (*15–17*). Other patients living with cancer do receive timely intervention, but treatment is basic. With regard to cancer medicines, cancer patients usually only receive basic chemotherapy. Finally, a much smaller proportion of cancer patients do receive state-of-the-art cancer care, including the use of newer high-cost cancer medicines. These patients mostly live in high-income countries, or belong to the highest socioeconomic group.

These statistics are a constant reminder to the global community that solving the multitude of problems associated with cancer will continue to require strong cross-sectoral commitments, and with actions across all areas of cancer care. Commitments to the policy mandates stipulated in the Sustainable Development Goals[ii] and the World Health Assembly resolution on cancer prevention and control are therefore particularly pertinent.

Actions across all areas of cancer care are needed

1.1.2 High prices and growing expenditure on cancer medicines

The aspiration of delivering sustainable cancer care as part of universal health coverage in recent years has been challenged by two notable issues: the high prices of cancer medicines, and the growing expenditure on cancer medicines at rates higher than the growth rates in patient population and overall health expenditure.

In 2017, estimated global expenditure on medicines for cancer and related supportive care (e.g. anti-emetics, haematopoietic growth factors) amounted to US$ 133 billion (*18*). Compared to the global expenditure of US$ 90.9 billion in 2012 (*19*), the annual compound growth rate for cancer medicine spending was 7.9%. The fastest growth in spending was in the United States of America, where expenditure grew at a rate of 10.3% annually from US$ 32.5 billion in 2012 to US$ 52.1 billion in 2016[iii] (*19*). Such trends have also been noted at various regional, country and health service levels (*20–23*).

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[i] Country groups come from the World Bank: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519

[ii] Two SDGs are relevant to cancer prevention and control: **SDG 3.4**: By 2030, reduce by one third premature mortality from non-communicable diseases, including cancer, through prevention and treatment and promote mental health and well-being; **SDG 3.8**: Achieve universal health coverage, including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all.

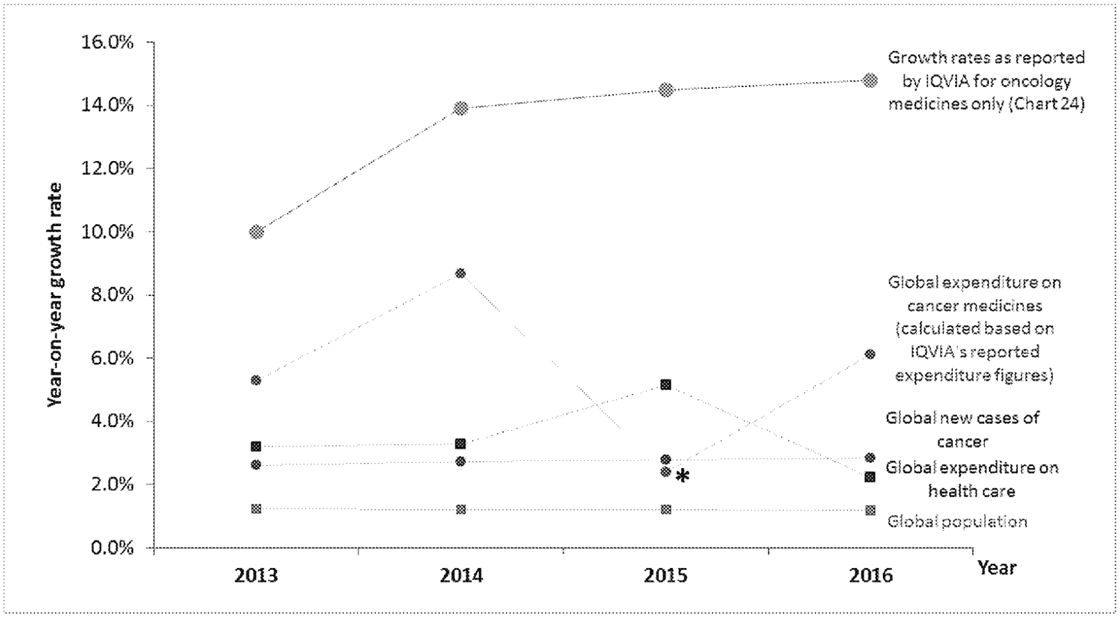
[iii] Disaggregated data by country and region were not available for 2017.

The expenditure on cancer medicines grew at rates (5.3–8.7% per year) higher than the growth rates of people newly diagnosed with cancer (2.6–2.8% per year) globally during 2012–2016[iv] (Fig. 1.1, p.3). While increased use of cancer medicines might have contributed to the growing expenditure as suggested by historical trends in some health care contexts (*24–26*), the increased spending on cancer medicines was likely to be due to increases in medicine prices or a shifts towards using higher-cost cancer medicines.

> *Expenditure on cancer medicines has grown at rates higher than the growth rates in patient population and overall health expenditure*

Furthermore, the expenditure growth for cancer medicines was higher than the growth of overall health care expenditure (Fig. 1.1). Over 2012–2016, the per-capita expenditure on cancer medicines has been about 2- to 8-fold above the overall per-capita expenditure on health, when using new cases of cancer as a proxy for treatment population (Fig. 1.2a, p.3). When using the prevalent cases as a proxy for treatment population (i.e. including patients who are off treatment during remission), the ratios of per-capita expenditure between cancer medicine and health care remain above 2 globally except in the United States and Japan (Fig. 1.2b). The difference was particularly stark in regions with a large proportion of lower-income countries. This suggests that expenditure on cancer medicines may be disproportionately high, to the extent that cancer medicines may potentially displace resources for the management of other health conditions if the overall health care budget is maintained at the same level.

Fig. 1.1: Year-on-year growth rates of expenditures on cancer medicines and health care

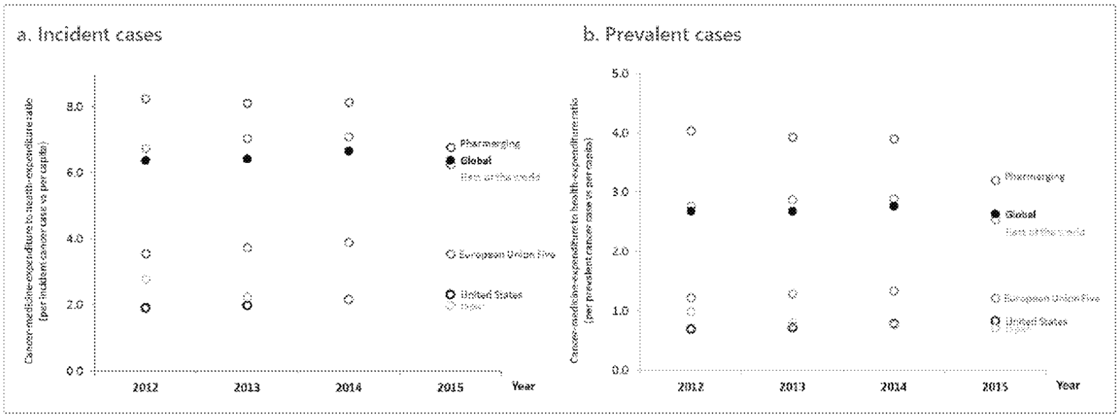


Note: Cancer medicines include medicines for the treatment of solid tumours and blood cancers as well as for supportive care such as anti-emetics, erythropoietins, haematopoietic growth factors, select interferons, bisphosphonates. The growth rates reported by IQVIA Institute for Human Data Science only related to oncology therapeutics, without supportive care.

Source: Author's calculations based on data from the WHO Global Health Expenditure Database (*27*) and IQVIA Institute for Human Data Science (*19*)

[iv] The large drop in the growth rate in 2015 cancer medicine expenditure (calculated by IQVIA based on variable exchange rates) was possibly an artefact of the currency conversion method, when the US dollar strengthened significantly against all other major currencies in 2015.

Fig. 1.2: Comparison of expenditures on cancer medicines and health based on per-capita expenditures, by (a) incident cases and (b) prevalent cases



Note: 'Pharmerging' is a group of 21 countries with less than US$ 30 000 GDP per capita and greater than US$ 1 billion in the growth of sales for prescription medicines between 2014 and 2019, as defined by the data source: China, Brazil, India, Russian Federation, Mexico, Turkey, Poland, Saudi Arabia, Indonesia, Egypt, Philippines, Pakistan, Viet Nam, Bangladesh, Argentina, Algeria, Colombia, South Africa, Chile, Nigeria, Kazakhstan. European Union Five includes France, Germany, Italy, Spain and the United Kingdom of Great Britain and Northern Ireland

Source: Author's calculations based on data from WHO Global Health Expenditure Database (*27*) and IQVIA Institute for Human Data Science (*19*)

1.1.3 Stakeholder reactions and governments' responses

The growing expenditure and high prices of cancer medicines have attracted an extensive body of commentary from diverse stakeholders in recent years. Stakeholders at all levels – from patients and clinicians to governments – have expressed their concerns that such high prices would compromise the availability and affordability of these medicines to patients, as well as the sustainability of health systems.

For example, in 2011, the Lancet Oncology Commission on Global Cancer Surgery called for a "radical shift in cancer policy" and that "cancer profession and industry should take responsibility and not accept a substandard evidence base and an ethos of very small benefit at whatever cost; rather, we need delivery of fair prices and real value from new technologies" (*28*). In 2012, an article published in the New York Times highlighted that ignoring the cost of cancer treatment was "not tenable" (*29*). In 2013, a group of more than 100 experts in chronic myeloid leukaemia pointed to the fact that 11 of the 12 medicines approved by the United States Food & Drug Administration (US FDA) in 2012 for various cancer indications were priced above US$ 100 000 per year. The experts asserted that the prices of these medicines were too high, unsustainable, might compromise access of needy patients to highly effective therapy, and harmful to the sustainability of national health care systems (*30*). Similarly, in 2015, yet another group of cancer experts have petitioned for lower medicine prices (*31*).

> *Stakeholders have voiced concerns about a lack of adequate access to cancer medicines due high costs*

Despite the chorus of concerns, existing regulatory and non-regulatory measures do not seem to have suitably resulted in outcomes that meet both policy and economic objectives, as well as public expectations. Stakeholders continue to voice their concerns about the lack of adequate access to both new and off-patent essential cancer medicines. Furthermore, the prices of cancer medicines continue to rise significantly, possibly disproportionally to the benefits conferred and to the extent that the financial sustainability of health care systems are genuinely compromised (*32–39*). These concerns have culminated in a number of reviews at international (*40–43*) and country levels (*44–49*). Some common themes in these reviews are:

- seeking better alignment of prices and the costs associated with the use of cancer medicines, with their health benefits in clinical practice compared to alternative medicines;
- enforcing greater transparency on the prices of cancer medicines and the costs of research, development and production;
- correcting the imbalance on the negotiating powers between payers and manufacturers;
- enhancing the use of generic and biosimilar cancer medicines with a view to enhancing competition; and
- ensuring that the application of patent law and rights for market exclusivity are not over-compensating innovators and becoming barriers to access.

1.1.4 A balanced approach to improve patient access to cancer care

It is important to reiterate from the outset that suboptimal access to cancer medicines is only one of the many challenges relating to people's access to appropriate cancer care (*50*). Patient access to adequate care depends on a range of factors such as financial resources, insurance coverage, availability and skill set of health workforce, health care infrastructure and physical access to health services. As these factors are inextricably linked, many problems and challenges related to the provision of cancer medicines are likely to be common across other parts of the health care system. For example, an analysis of the literature and insights from key informants found that "the cancer economics debate has largely centred on the provision of drugs, with access to radiotherapy and over-penetration of high-cost radiation technologies under-represented in media outputs and political discussion" (*51*). Further to this point, there is evidence that access to adequate cancer care other than access to cancer medicines remains inequitably distributed between and within countries (*52,53*). For all these reasons, a nation's investment in cancer control needs to consider the full spectrum of interventions from prevention to palliation. For many countries, there will be greater return on investment in cancer control from improving access to preventative interventions (e.g. vaccines for hepatitis B virus or HPV) or better surgery, than from access to newer cancer medicines of marginal clinical benefits and non-fully established safety profile.

> *A nation's investment in cancer control needs to consider the full spectrum of interventions from prevention to palliation*

It is also worth noting that the public often sees cancer as distinctive perhaps because of the severity of the disease and the strong emotion it evokes. However, empirical evidence does not always consistently support a preference for health gains in cancer compared to other health conditions (*54*). Therefore, charting a course for reform to improve people's access to cancer medicines ought to be considered across the entire health sector, such that the benefits of improving access to cancer medicines would not be at the expense of essential health care products and services for other disease areas.

1.2 Purpose of this report

In view of the resolution and with consideration to the context of cancer care, this report seeks to clarify the following questions.

- What are the objectives of an optimal pricing policy with consideration to the context of cancer medicines?
- What are the approaches used for pricing cancer medicines?
- What are the impacts of these pricing approaches on the affordability and availability of cancer medicines?
- What are the potential unintended consequences of pricing policies, or the lack thereof?
- What are the potential options that might enhance the affordability and accessibility of cancer medicines?

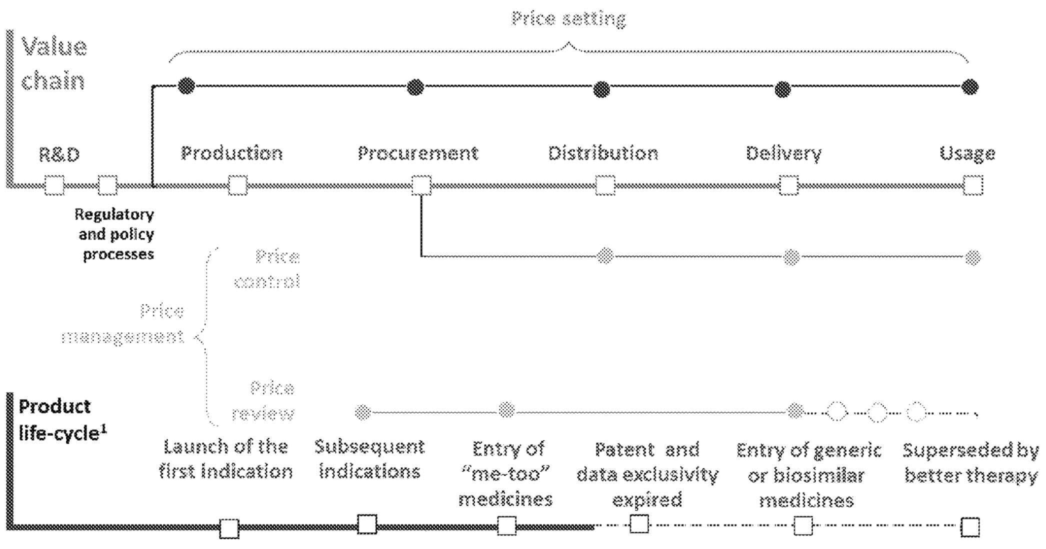
1.3 Scope and methods

1.3.1 Scope

This report considers "cancer medicines" as medicines for the prevention and treatment of both solid tumours and haematological cancers in both adult and paediatric settings. The report has a particular focus on medicines listed on the 2017 World Health Organization (WHO) Model List of Essential Medicines (EML) as well as high-cost cancer medicines recently introduced to the market.

The report considers pricing approaches (and reimbursement policies) used for setting and managing the prices of cancer medicines at various points along the value chain, as well as different time-points throughout the product life-cycle of cancer medicines, as illustrated in Fig. 1.3 (p.6). It also presents specific discussions on the costs and incentives for undertaking research and development (R&D) of cancer medicines.

Fig. 1.3: Points along the value chain and product life-cycles for price setting and management


Price setting
Value chain
R&D
Production
Procurement
Distribution
Delivery
Usage
Regulatory and policy processes
Price control
Price management
Price review
Product life-cycle¹
Launch of the first indication
Subsequent indications
Entry of "me-too" medicines
Patent and data exclusivity expired
Entry of generic or biosimilar medicines
Superseded by better therapy

● **Possible points for setting prices along the value chain:** i.e. ex-manufacturer, ex-distributor/wholesalers, ex-service providers, and consumer

▨ **Possible points for price control and review:** point in time when there is a change in market dynamics (e.g. additional indications and entries of substitutes)

Note: [1] Product life-cycle refers to the different stages of the product from introduction, growth, maturity or stabilization and decline in market share. The diagrams are indicative and not to time scale

For the purpose of this report, potential impacts of pricing policies are discussed from the perspective of the health system according to the following definitions as reported in the literature, or based on common understanding of the terms.

- **Availability**: Presence of medicines in national formulary available to patients for free or for a fixed fee (*35,55,56*);
- **Affordability**: for the health system – Proportion of spending on cancer medicines compared to existing expenditure on medicines or other health products and services; for individual patients – The number of days' wages needed to pay for the cost of treatment (*56*).
- **Transparency**: The disclosure and dissemination of information to relevant parties to ensure accountability. For example, price transparency refers to disclosure of the net transaction prices of cancer medicines between the sellers (e.g. manufacturers, service providers) and the payers/buyers (governments, consumers) (cf. list prices in pricing catalogue or on invoice prior to applying discounts).
- **Unintended consequences**: Unplanned outcomes arising from planned actions that have deviated from the original intent. The effects of these unplanned outcomes could be positive, potentially problematic or negative. These effects may reduce the occurrence or magnitude of the anticipated outcomes (e.g. health outcomes or expenditure).

1.3.2 Methods

The methods for preparing this report comprise five components, discussed below.

1.3.2.1 Targeted review of policy documents and literature

A targeted review of literature (empirical and grey literature) and databases was undertaken to identify relevant information for this report, with a view to undertaking exhaustive narrative synthesis of extant documents. Websites and databases from which data and information were extracted include:

- Bibliographic and informational databases
  - US National Library of Medicine's PubMed database
  - WHO Global Cancer Observatory
  - WHO Global Health Expenditure Database
  - Institute for Health Metrics and Evaluation's Global Health Data Exchange
  - Pricing databases hosted by country authorities and organizations
- Websites of relevant national and international organizations or initiatives
  - WHO Headquarters and regional offices
  - The Organisation for Economic Co-operation and Development (OECD)
  - The European Commission
  - Country authorities responsible for the provision and pricing of cancer medicines.

WHO regional offices were contacted directly to obtain any non-publicly available reports relating to the scope of this report.

1.3.2.2 Examples and case studies

This report presents case studies to complement the discussion. In general, these case studies and examples pertain to pricing approaches of cancer medicines used in different countries, and where available their impacts; and the discovery and R&D pathway and sources of research funding of cancer medicines.

1.3.2.3 Quantitative analyses

This report also presents the findings of a range of quantitative analyses. The specific methods and sources of data for these analyses are described in the relevant sections of this report.

1.3.2.4 Informal advisory groups of experts

To assist with the preparation of the report, the Secretariat convened meetings with two groups of technical experts: the Essential Medicine List Cancer Medicines Working Group (EML Working Group), and an Informal Advisory Group on Availability and Affordability of Cancer Medicines (Informal Advisory Group).

The EML Working Group, the members of which were nominated by the WHO Expert Committee on Selection and Use of Essential Medicines, was consulted on 22–23 March 2018 about: (a) magnitude of benefit of new cancer medicines; (b) recent trends in trial design; and (c) how to identify treatments that offer high clinical and public health value. The Informal Advisory Group, the members of which were nominated by WHO regional offices, was consulted on 4–6 April 2018 to: (a) provide technical guidance on scope of the report, analytical feasibility and case studies; (b) clarify benefits and consequences of various pricing approaches for cancer medicines; and (c) suggest options that might improve affordability and accessibility of cancer medicines.

Appendix C presents the lists of meeting participants. The agenda and minutes of these meetings are published on WHO websites[v]. The expert meeting participants provided advice and comments on the drafts of this report.

1.3.2.5 Information session for Member States

On 31 July 2018, the Secretariat hosted an information session at WHO headquarter in Geneva with representatives of the Permanent Missions of Member States. Representatives from 24 Member States attended the session. At the meeting, the Secretariat briefed the participants about the processes for preparing the report, and its scope of content. The views expressed by Member States at this meeting were considered by the Secretariat during the writing of the report.

1.4 Report structure

This report presents the following information:

- **Chapter 2 presents a brief discussion on the benefits of cancer medicines**, with a view to setting the discussion on pricing of cancer medicines within the context of their clinical benefits. It focuses on recently approved medicines that target specific cancer-related molecular alterations (i.e. targeted cancer medicines).

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[v] http://apps.who.int/iris/bitstream/handle/10665/272962/WHO-EMP-IAU-2018.03-eng.pdf?ua=1
http://apps.who.int/iris/bitstream/handle/10665/272961/WHO-EMP-IAU-2018.04-eng.pdf?ua=1

- **Chapter 3 discusses various pricing approaches of cancer medicines** adopted by the pharmaceutical industry and authorities responsible for the regulation of medicine prices. The discussion presents information and analysis on various components of the value chain, with a view to establish any observable relationship between inputs to value chain and the prices of medicines.
- **Chapter 4 examines the impacts of pricing approaches** on medicine prices, availability, affordability, research and development, transparency and unintended negative consequences from the perspective of the health care system.
- **Chapter 5 concludes this report** by presenting options that might enhance the availability and affordability of cancer medicines.

2 Benefits and risks of cancer medicines

Pricing of cancer medicines is often discussed within the context of their benefits. To this end, this chapter describes briefly the current discourse on the benefits of newer cancer medicines. It also presents the recommendations from the meeting of the EML Working Group.

2.1 Evidence of benefits and risks of newer cancer medicines

In the 1940s, the advent of chemotherapy provided clinicians with a therapeutic option in addition to radiation therapy for treating patients with cancer. Over the next eight decades, there has been much progress in the pharmacological treatment of cancer, including understanding hormone dependence of normal and cancer cells, development of chemotherapy after surgical intervention, and the use of combination chemotherapy (*57*). Chemotherapy remains the mainstay of cancer pharmacological treatment.

More recent progress towards contemporary pharmacological treatment of cancer has been substantive on at least two fronts. Firstly, advances in molecular biology, genetic and genomic science over the past decades have allowed for a better understanding of cancer at an unprecedented level of detail. Researchers have identified a vast range of mutations in cancer-associated genes, including BRCA, HER2, EGFR, BRAF, KRAS, ALK, PDL, to name a few (*58*). This means that, based on specific genetic profiles, clinicians can better identify individuals with higher risks of developing cancer and patients with poorer disease prognosis. Secondly, building on better understanding of the molecular characteristics of cancer, researchers have developed medicines that can mitigate the negative effects of genetic mutations with a greater level of selectivity. By 2018, the US FDA has approved more than 90 cancer medicines on the basis of evidence of benefit for patients with specific genetic characteristics – termed targeted therapies (*59*). Other development includes the introduction of immunotherapy and the quantification of the total number of mutations within an area of the cancer genome (i.e. tumour mutational burden) to predict treatment response.

> *Scientific advances over past decades have improved our understanding of cancer and transformed patient care*

Together with the improvement in overall cancer care (i.e. detection, surgery, radiotherapy, pharmacological treatments and other supportive care), patients with cancer in many countries today receive more effective treatments with better managed toxicity than in the previous decades. This has translated to improved survival, as shown in the increasing trend during the 15-year period from 2000 (Appendix B) (*11*). It should be emphasized that the improved survival for patients with some solid cancers were attributable mostly to early diagnosis, and improvements in pathology, imaging, radiotherapy and surgical interventions (*60,61*). Cancer medicines have contributed to site-specific improvements in survival for specific cancers, such as haematological cancers and usage in specific regimens in adjuvant setting (i.e. after surgical intervention or radiotherapy).

2.1.1 Magnitude of benefits and risks

Treatment with some cancer medicines clearly leads to substantial improvements in health outcomes. Their adoption in clinical practice has transformed patient care for several cancer types. These include imatinib for chronic myeloid leukaemia, rituximab for non-Hodgkin lymphoma, trastuzumab for early-stage and metastatic breast cancer, to name a few. The evidence is well documented in the literature, and will not be replicated here.

In contrast, there are an increasing number of clinicians who question the benefits of some newer cancer medicines in extending and improving the life of cancer patients, compared to standard of care. Specifically, they are concerned that many cancer medicines have received regulatory approvals in the past decades on the basis of surrogate end-points[vi], with insufficient evidence of benefits on clinical outcomes (*62–68*).

An increasing number of clinicians question the benefits of some newer cancer medicines

A systematic evaluation of 68 cancer medicines approved by the European Medicines Agency (EMA) in 2009–2013 showed that only 35% had established evidence of prolonged survival at the time of approval (*64*). Similarly, only 10% of the 68 medicines had evidence of improvement in the quality of life at the time of approval. Furthermore, only an additional three approved medicines/indications subsequently reported benefits in prolonging survival and an additional five medicines in improving quality of life during the post-marketing period of at least 3.3 years (*64*). This observation is consistent with the findings of another study that examined the approvals of cancer medicines by the US FDA from 2008–2012: only 18 (33%) of the 54 approvals were granted on the basis of prolonged survival, with only five additional medicines subsequently shown to have improved overall survival during the post-marketing period (*62*).

For medicines that have been found to improve survival, the above studies also demonstrated that the overall magnitude of benefits was often weeks or a few months. Of the cancer medicines approved by the EMA on the basis of extended survival, the overall survival was extended for a median 2.7 months (range: 1.0 month to 5.8 months) (*64*). Another study on US FDA-approved medicines for solid tumours between 2002 and 2014 also found modest progression-free and overall survival gains of 2.5 months and 2.1 months, respectively (*69*).

There are also concerns about the safety profile of newer cancer medicines

There are also concerns about the safety profile of newer cancer medicines. Despite their targeted mechanisms of action, a systematic review found that the odds of toxic death were greater for newer targeted agents than control (OR=1.40; 95% CI: 1.15–1.70; $P<0.001$). The odds of treatment-discontinuation were also higher (OR=1.33; 95% CI: 1.22–1.45, $P<0.001$) (*70*). This study questioned the trade-offs between efficacy and toxicity in clinical practice because patients in clinical practice typically have lower performance status and higher number of comorbid conditions.

[vi] Surrogate end-points are "outcome measures that are not of direct practical importance but are believed to reflect outcomes that are important" (*410*). In cancer research, surrogate end-points include tumour response rate or progression-free survival.

Some examples of cancer medicines with marginal benefits and potential harms, as noted by cancer experts in published literature (*69,71*) , are listed for illustrative purpose in Table 2.1.

Table 2.1: Examples of medicines with marginal benefits and potential harms

Intervention	**Indication**	**Comparator**	**Magnitude of benefits**	**Adverse events**
Cetuximab with FOLFIRI (irinotecan, 5-fluorouracil, leucovorin) (*72*)	First-line treatment in KRAS mutation-negative EGFR-expressing metastatic colorectal cancer	FOLFIRI alone	Median PFS • 8.9 months vs 8.0 months • HR= 0.85 (*P*=0.048) Median OS • 19.9 months vs 18.6 months • HR= 0.93 (*P*=0.31)	Any events • 79% vs 61% (*P*<0.001) Acne-like rash • 16.2% vs 0% (*P*<0.001) Infusion related • 2.5% vs 0% (*P*<0.001)
Bevacizumab with paclitaxel and carboplatin (*73*)	First-line treatment of locally advanced, recurrent, or metastatic non-squamous non-small-cell lung cancer	Paclitaxel and carboplatin alone	Median PFS • 6.2 months vs 4.5 months • HR= 0.66 (*P*<0.001) Median OS • 12.3 months vs 10.3 months • HR= 0.79 (*P*=0.003)	Neutropenia • 25.5% vs 16.8% (*P*=0.002) Thrombocytopaenia • 1.6% vs 0.2% (*P*=0.04) Bleeding events • 4.4% vs 0.7% (*P*<0.001)
Bevacizumab with paclitaxel (*74*)	Metastatic breast cancer	Paclitaxel alone	Median PFS • 11.8 months vs 5.9 months • HR= 0.60 (*P*<0.001) Median OS • 26.7 months vs 25.2 months • HR= 0.88 (*P*=0.1)	Hypertension • 14.8% vs 0.0% (P<0.001) Proteinuria • 3.6% vs 0.0% (P<0.001) Cerebrovascular ischaemia • 1.9% vs 0.0% (*P*= 0.02)
Erlotinib with gemcitabine (*75*)	First-line treatment of patients with locally advanced, unresectable or metastatic pancreatic cancer	Gemcitabine alone	Median PFS • 3.75 months vs 3.55 months • HR= 0.77 (95% CI: 0.64–0.92) Median OS • 6.24 months vs 5.91 months • HR= 0.82 (95% CI: 0.69–0.99)	Rash • 72% vs 29% Infection • 43% vs 34% Interstitial lung disease-like syndrome • 2.1% vs 0.4%

Intervention	Indication	Comparator	Magnitude of benefits	Adverse events
Ramucirumab (*76*)	Metastatic or unresectable, locally recurrent gastric or gastro-oesophageal junction adeno-carcinoma	Best supportive care	Median PFS • 2.1 months vs 1.3 months • HR= 0.48 (95% CI: 0.38–0.62) Median OS • 5.2 months vs 3.8 months • HR= 0.77 (95% CI: 0.60–1.00)	Hypertension • 16% vs 8% Haemorrhage • 13% vs 11%
Neratinib, administered after chemo-therapy and trastuzumab (*77*)	The extended adjuvant treatment of adult patients with early stage HER2-over-expressed/ amplified breast cancer	Placebo, administered after chemo-therapy and trastuzumab	5-year invasive disease-free survival • 90.2% vs 87.7% • HR= 0.73 (95% CI: 0.57–0.92)	Grade 3 diarrhoea • 40% vs 2% Vomiting • 3% vs <1% Nausea • 2% vs <1%

Note: HR= Hazard ratio; PFS=progression free survival, OS=overall survival

Source: (*72–77*)

2.1.2 Translation of trial evidence in clinical practice

Even with sufficient clinical trial evidence at the time of regulatory approval, it is important to recognize that the benefits may not be realized in clinical practice because of a range of reasons, such as bias in measuring outcomes in clinical trials or underreporting of adverse events (*78*).

For newer targeted cancer medicines, there are two additional areas of uncertainty. Firstly, despite their established mechanisms of action, targeted cancer medicines may not have clinically-meaningful activities against all tumours with a matching genetic mutation. To this point, a clinical trial has found that the progression-free survival of patients with metastatic solid tumour refractory to standard of care did not improve with the use of targeted therapies that matched with the tumour's molecular profile but outside their approved indications, compared to patients who received treatment at the choice of their treating physicians (*79*). This means that targeted therapies should only be used according to approved indications and not based on identified molecular alternations or the general type of cancer.

> *Outcomes observed in clinical trials may not translate into benefits for patients in clinical practice*

Secondly, a major limitation of targeted cancer medicines is the occurrence of treatment resistance which can result in a lack of response (termed intrinsic resistance) or partial or loss of responses over time (termed acquired resistance) (*80*). Clinically, this means that patients may experience prolonged progression-free survival, but not improved overall survival. While researchers continue to unravel the complex mechanisms of and mitigation strategies for treatment resistance, it is important to recognize that the use of single targeted therapies may not have durable treatment effects in clinical practice. Furthermore, while the use of targeted therapies in combination may in theory mitigate the emergence of treatment resistance (*81*), safety consideration either preclude the use of such combination, or compromise the doses at which individual agents could be used in combination, which might in turn lower its efficacy (*82*).

2.2 Opinion of the EML Cancer Medicines Working Group

On 22–23 March 2018, the EML Cancer Medicines Working Group discussed extant evidence on the magnitude of benefits of cancer medicines. The Working Group also shared country experience in facilitating access to existing cancer medicines on the EML, newer high-cost cancer medicines and cancer care in general. Below is a summary of the main points presented and discussed in the meeting (*83*).

The Working Group discussed that in the past 15–20 years many cancer medicines were granted marketing rights on the basis of improvement in surrogate end-points, often in the absence of further evidence to demonstrate their benefits in extending or improving life. The group expressed concern regarding a lack of robust correlation between surrogate end-points and patient outcomes in clinical practice. It also highlighted that some newer medicines may expose patients to higher risk of toxicities. Also discussed were various sources of biases from trial methodology, including censoring, early reporting and ascertainment bias.

In view of the issues, the Working Group expressed a need to set a robust evidentiary requirement to indicate clinically meaningful outcomes that should be expected from cancer medicines in order to be considered for inclusion in the EML, with a view to supporting countries selecting cancer medicines of higher clinical value. To this end, the Working Group advised WHO to use an overall survival interval of at least 4 months for first-line treatments as a general guiding principle for considering medicines for inclusion in the EML. For medicines with limited data on survival, evidence of disease-free or progression-free survival may be considered on a case-by-case basis, provided that the benefits are large, validated and consistent with other evidence. In considering these recommendations, the Working Group noted the following points:

- overall survival of less than 3 months would generally be considered as marginal and might not be relevant from both clinical and ethical perspectives;
- due to methodological biases, findings from clinical trials have the tendency to overestimate the likely benefits of cancer medicines when used in clinical practice. The usefulness of a medicine might also be impaired because of differences in the characteristics of patient populations and health care settings, including the capacity of health services in low- and middle-income countries in delivering medicine according to best practice and managing drug-related toxicities.

The Working Group considered the rating scales developed by the American Society of Clinical Oncology (ASCO's Value Framework) and the European Society for Medical Oncology (ESMO's Magnitude of Clinical Benefit Scale or MCBS) to facilitate the benefit assessment process. It agreed that both scales could be used but they expressed a preference for the scale by ESMO because:

- ESMO-MCBS allows assessment of benefits in relative and absolute terms. This is consistent with the requirements of the EML Expert Committee;
- ESMO is a nongovernmental organization (NGO) in official relationship with WHO;
- all newly approved cancer medicines since 2016 has been evaluated using ESMO-MCBS; and
- ESMO plans to expand the MCBS to cover medicines for haematological malignancies in collaboration with the European Haematological Society.

The Working Group suggested that medicines with a score of 4 and 5 or a rating of A and B on the ESMO-MCBS could be considered eligible for consideration for EML listing, provided that clinical evidence demonstrated at least 4 months of additional overall survival compared to standard care. The Working Group acknowledged that ESMO-MCBS did not fully account for toxicity profile and therapy discontinuation when considering the risk–benefit profile. For these reasons, all cancer medicines seeking listing on the EML will require full assessment of evidence, including consideration of generalizability of the evidence at the global level.

2.3 Summary

This brief chapter noted some of the contemporary discussion in the literature regarding the magnitude of benefits for newer high-cost cancer medicines.

i. The development of cancer medicines since the discovery of chemotherapy in the 1940s has been remarkable. Some medicines have demonstrated substantial improvements in health outcomes and have transformed patient care for several cancer types.
ii. However, in the past 15–20 years, a considerable proportion of targeted therapies received marketing approvals based only on improvement in surrogate end-points demonstrated in clinical trials, often in the absence of further evidence to demonstrate their benefits in extending or improving life in clinical trials and clinical practice.
iii. For medicines that have shown survival advantages, the overall magnitude of benefits was considered marginal at around 3 months. Some medicines may present higher risk of toxicities to patients.
iv. The use of targeted therapies based on identified molecular alterations outside of approved indications should be discouraged, in line with the extant evidence.

3 Pricing approaches for cancer medicines

This chapter provides an overview of various approaches adopted by government authorities and pharmaceutical companies for the pricing of medicines in general. It examines inputs throughout the value chain and price setting. Where possible, it discusses the pricing approaches with examples specific to cancer medicines.

3.1 Objectives of national pricing policy and pricing approaches

Many countries have implemented national medicines policies to guide and coordinate context-specific actions towards achieving long-term goals for the pharmaceutical sector (*84*). Pricing policy is often one main part of the overall policy. The specific goals of the national medicine policies, and their sub-policies (e.g. pricing policy), may vary according to the structure and capacity of the health care systems (*84*). However, the core of national medicine policies and their sub-policies generally follow some common principles.

Firstly, national medicines policies often include the following **health system-related goals** (*84*):

- to ensure timely and equitable patient access to affordable medicines with established safety, efficacy and quality;
- to improve prescribing and dispensing practices;
- to promote ethical practices among medicine suppliers and health professionals; and
- to ensure system transparency with clear lines of accountability.

In addition, medicine policies in some countries may have explicit **economic goals**, such as:

- to achieve prices of medicines that are financially sustainable to patients and individuals;
- to promote efficiency for the administration of the policies;
- to enhance competition in the pharmaceutical sector;
- to promote innovation in developing better therapies; and
- to support the development of a responsible and commercially-viable pharmaceutical industry.

Applying this broad framework to the context of cancer medicines, an optimal pricing policy should facilitate the supply of cancer medicines to patients in need, in a fair and timely manner without compromising the quality and safety of medicines. It must ensure overall affordability to individual patients with cancer over the full course of treatment. A health system must also be able to maintain its financial sustainability so that spending on cancer medicines would not divert resources required for the provision of other essential health products and services.

In line with the principles of good governance, pricing policy and approaches may consider complying with the notion of transparency. That is, the policy may consider adequate disclosure of price information to the market, with a view to promoting efficiency through information symmetry and ensuring accountability.

Pricing policies should provide sufficient financial incentives and rewards to ensure sustainable supply and the commercial viability of pharmaceutical manufacturers and other providers of goods and services along the value chain. This is pertinent considering the contribution of the pharmaceutical industry on the local and global economy, particularly in countries where there is significant presence of pharmaceutical industry. Furthermore, in the long term, it should motivate, through policy structure and financial incentives, research organizations in public and private sectors towards developing new cancer medicines with clinically meaningful benefits. Such policies may align the incentives towards areas with high public interest (e.g. cancers with high burden of disease) or expectations (e.g. severe and rare cancers and childhood cancers).

3.2 Industry's pricing approaches

Ascertaining the specific pricing strategies and approaches used by pharmaceutical companies is difficult because it requires access to proprietary information regarding inputs to the value chain. Pricing strategies and approaches are also likely to vary by company, the characteristics of cancer medicine and the market context. Nonetheless, this section documents some of the pharmaceutical industry's stated determinants of medicine prices along the value chain, as noted in public sources. This is followed by a discussion on the characteristics of the market for cancer medicines, with a view to explaining some of the behaviours of pharmaceutical companies based on known economic principles.

3.2.1 Relationship between inputs throughout value chain and price setting

The pharmaceutical industry and various commentators have noted four determinants of medicine prices: (1) costs of R&D; (2) costs of production and other expenditures relating to product commercialization; (3) value of medicine to patients, health care system and society; and (4) sufficient financial returns to incentivize future R&D programmes (*85–89*). These factors are examined in turn below.

3.2.1.1 Covering past R&D costs

The first stated rationale from the industry is that the prices of medicines must consider *all* R&D expenses. To this point, the industry has argued that the prices of medicines must account for not only the R&D costs of the approved medicine, but also expenditures on investigating drug candidates for which marketing approvals did not eventuate. In other words, the industry has argued that medicine prices should account for the costs of failed attempts in R&D (*85–87*). Furthermore, the industry has inferred that medicine prices should include the "cost of capital", that is, the potential financial returns had the money been used in other areas of investment with equal risk to drug development (i.e. the opportunity cost) (*90,91*).

The true costs of R&D for pharmaceuticals, including for cancer medicines, are unknown and highly variable

Attempts to quantify the R&D costs of developing an approved medicine to date have resulted in estimates with significant variation. Depending on the study scope and methodology, the estimated R&D costs for developing one new medicine range from US$ 100 million to US$ 4.2 billion (*90–98*). For example, one oft-cited study estimated that the risk-adjusted cost of R&D for one market-approved medicine was US$ 2 558 million in 2013 dollars (*91*). This study collected data from multinational pharmaceutical companies through a confidential (unverifiable[vii]) survey. It linked the costs of failed medicines to the costs of the successful medicines through time-expenditure profile. This study also adjusted the financial estimates for the cost of capital by incorporating a rate of return of 10.5% per year (*91*). In contrast, another study found that the median cost for developing a single cancer medicine, with adjustment for the cost of capital at 9% per year, was US$ 794 million in 2017 dollars (range: US$ 219 million–2 827 million) (*94*). This study was based on the cumulative R&D spending reported to the U.S. Securities and Exchange Commission for 10 cancer medicines approved by the US FDA in 2006–2015. By including only companies with no prior medicines approved for marketing in the USA market, this study removed the need for attributing costs across multiple approved medicines as in earlier studies.

[vii] For example, the identity and characteristics (e.g. size) of the pharmaceutical companies that participated in the survey was unknown. Furthermore, the analysis relied on data provided by the participating companies without clarifying the methods for identifying and counting R&D costs.

Both of these studies have drawn criticism regarding the methodology and findings. The critiques have included questions about the dataset's representativeness, time frame and validation; the appropriateness of incorporating the cost of capital; the methodology for addressing tax credits that companies had received from governments for undertaking R&D; and the flexibilities in assigning expenses to different cost categories at the firm's discretion despite being compliant to the United States Generally Accepted Accounting Principles as required by law (e.g. *53,54*). In the absence of directly observed financial costs of R&D for drug discovery and consistent reporting, any further modelling studies based on publicly-available aggregated data or non-transparent confidential data are arguably not likely to yield more robust estimates.

Irrespective of the true magnitude of R&D costs, it can be inferred that current prices of (and profits from) cancer medicines are at least sufficient to account for, if not in excess of, the risks inherent in the R&D of cancer medicines. The returns are also sufficient for what would be necessary for the industry to maintain operation and continue to undertake R&D activities, as evident in the high proportion of compounds in development for cancer (*99*). These inferred assertions are supported by analysis presented in Sections 3.2.1.5 and 4.4.

In other words, the current pricing of cancer medicines has considered all risks of R&D and profit expectation. This is especially the case when the public and non-profit-making sectors have made considerable contributions towards the R&D of medicines (See Section 4.4). The industry has argued for having "a public policy environment that recognizes and rewards risk taking" (p.23) (*87*). A pertinent question for all stakeholders to consider is whether such expectation for an essentially risk-free R&D and business model is in line with public interest for encouraging innovation and accountability. This point will be expanded further in Section 4.4 when considering the potential impacts of the current R&D model for cancer medicines.

> *An expectation from the pharmaceutical industry for an essentially risk-free R&D and business model may not be in line with public interest for encouraging innovation and accountability*

3.2.1.2 Costs of production

Medicine prices may also be a function of the costs of production. Costs of production are operating expenses relating to product commercialization, including regulatory compliance, manufacturing, distribution, marketing and sales, and general administration. The marginal costs of production refer to the additional costs associated with producing an additional unit of product.

It is generally accepted that the *marginal* costs of production of medicines are relatively small compared to their prices (*88*). This is supported by a number of studies on the marginal costs of production. For example, the Committee on Finance of the United States Senate reviewed the pricing of Sovaldi (sofosbuvir) – a medicine for the treatment of chronic hepatitis C virus infection that may prevent future cases of liver cancer. Based on internal company information, the review noted that Pharmasset – the originator of sofosbuvir – estimated the costs of commercial-scale manufacturing for a 12-week course of treatment would be only 0.9% and 1.5% of the total costs, if the treatment course were priced at US$ 50 000 and US$ 30 000, respectively (*100*). This finding is comparable to the results of another study which found that the production costs of four tyrosine kinase inhibitors for cancer treatment (US$ 128–4020 per person-year) were between 0.2% and 2.9% of the treatment prices (US$ 75 161–139 138) (*101*).

Furthermore, the marginal costs of production are likely to remain low over a wide range of quantities produced. This is based on empirical observations that the long-term marginal costs of production are likely to follow a reducing trend over a large span of outputs (*102–104*). Graphically, the long-term overall cost of producing one more unit is likely to follow an L-shaped curve over a wide range of outputs before it may rise due to diseconomies of scale. The theoretical explanation for the empirical observations is twofold: (1) the change in volume of output rises faster than the change in the costs of output; and (2) the change in volume would generally occur over time, thereby allowing management to adapt without causing diseconomies of scale (*102*). While this report did not identify empirical observation of the long-term cost curve for the production of pharmaceutical products, the marginal costs of producing cancer medicines may follow a similar trend.

The marginal costs of production are likely to remain low over a wide range of quantities of medicines produced

The existing cost structures of companies within the pharmaceutical industry vary considerably, with the costs of production – cost of goods plus selling, general and administrative expenses – account for around 50–70% of their total incomes (*105*). In pharmaceutical companies with market capitalization greater than US$ 10 billion, the cost of goods was proportionally much lower (19% of the total costs) compared to generic companies (41–45%) (Fig. 3.1, p.20). Across all company categories, expenses associated with selling, marketing and administration were between 25% and 31% of the total reported costs. A significant proportion of this expenditure might be for marketing and promotional activities (*106,107*). For example, a study found that in 2004 promotional activities in the USA accounted for 24.4% of the sales revenues[viii] (compared to 13.4% for R&D) (*106*). This raises the question of whether all such activities are necessary for disseminating scientific information about medicines, and whether reducing the costs of marketing would translate into a reduction in the costs and by extension prices of medicine.

Costs of promotional activities of medicines account for a large proportion of the expenses associated with selling, marketing and administration

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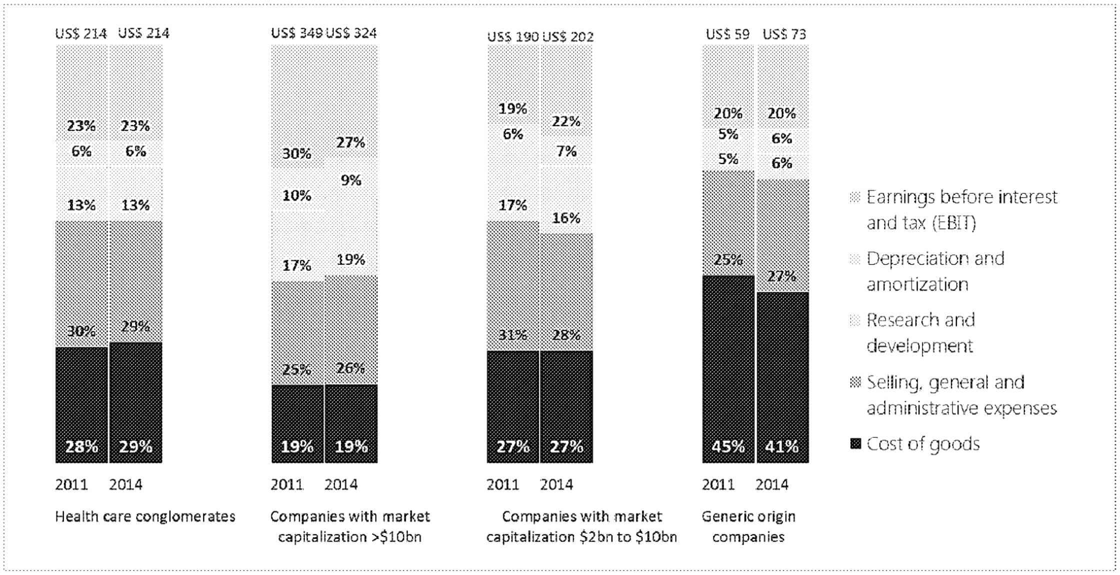
[viii] Revenue is the amount of monetary income a company receives, calculated by multiplying the per-unit net selling price of the goods (e.g. medicines) and the quantity of product sold.

Fig. 3.1: Cost structure of pharmaceutical and life science industry, by company type and year



Note: All non-percentage numbers are in billion

Source: Exhibit 2 in Gyurjyan et al. (2016) (*105*). (Reproduced with permission)

3.2.1.3 Determining the value of medicines

The third stated determinant of a medicine price is the value of the medicine. In countries where there is a process for assessing this term, the governments or authorized organizations consider the proposed price and costs of a medicine alongside scientific evidence demonstrating its health benefits and safety profiles. This is often done through a comparison against the next-best available therapeutic option(s). The assessment may also consider other locally relevant factors, such as disease patterns in the population and budgetary constraints, with a view to establishing the worthiness of that medicine within a specific context of use. As noted by an industry body:

> Industry works with governments in each Member State to establish a medicine's price that reflects the value it provides to patients and the healthcare system. Each government determines the value of a medicine based on a range of factors, including: impact on patients and their disease relative to other available treatments; potential to reduce other health care costs, such as hospital stays; individual country's health and economic needs. In addition to their local assessment of value, governments often use prices of other countries as a benchmark (*86*).

While the above description reflects the status quo in countries with a process for assessing the value of medicines, efforts to establish the price of a medicine according to its value (i.e. value pricing or value-based pricing) have had varying levels of reliability because of several sources of uncertainty. Firstly, the robustness of assessment framework and the capacity to undertake assessments vary significantly by country and authority (*108*). Secondly, as discussed in Chapter 2, many cancer medicines do not have well established evidence to inform their clinical and economic values at the time when they are being considered for regulatory and reimbursement approvals (*62,64,65*). These include a lack of data to demonstrate benefits in survival and well-being, as well as broader impacts, such as

Establishing medicine price according to its value has had varying levels of reliability the likelihood of generating financial savings through avoidance of hospitalization. Thirdly, the relative value of a medicine may appear to be very high when comparing against an inefficient current practice, even though the absolute magnitude of benefits of the medicine is low (i.e. marginal benefits). This pitfall is known as the so-called straw man comparison, which could result in prices higher than the true value. Finally, the conceptualization and measurement of value vary substantially because decision-makers, pharmaceutical companies and consumers often value various attributes of medicine differently (*109–111*). All these uncertainties present many challenges to the implementation of value-based pricing.

3.2.1.4 Achieving income expectation

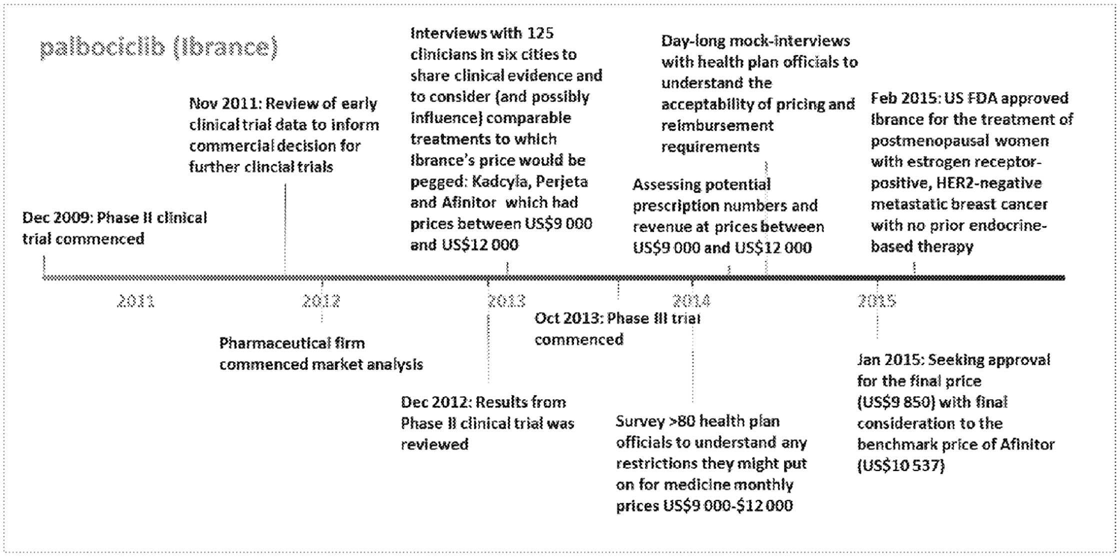
Instead of setting prices according to the value of medicines, pharmaceutical companies often place more emphasis on setting prices according to their income expectations (*88,100,112*). As noted by an executive of a major multinational firm, pricing of medicines is driven largely by the firm's consideration of "the cost of business, competition, patent status, anticipated volume, and, *most important* [emphasis added], our estimation of the income generated by sales of the product" (*88*). In other words, pricing of medicines is unconnected to either the relative or absolute therapeutic value of the medicines, or the costs of R&D and production. This point is supported by many price increases of cancer medicines over the past decades, where the only plausible explanation is the companies' attempt to reach their profit goals by setting prices as high as the market will bear. Examples include the following.

Companies often place more emphasis on setting prices according to their income expectations

- Prices of bevacizumab and trastuzumab were increased by 5% to 8% over two years from October 2012 in the USA without evidence of any changes to production costs or value of bevacizumab (*113*).
- Price of mechlorethamin – a treatment for cutaneous T-cell lymphoma – was increased from US$ 77.50 to US$ 548.01 in 2006 when it was licensed to a new firm, despite the fact that the originator firm continued the production of mechlorethamin for the new firm (*114*).
- The price of lomustine – a treatment for brain tumours, lung cancer and Hodgkin lymphoma – was increased by 1400% from US$ 50 in 2013 to $768 per capsule in 2017 following the sales of its marketing rights to a new firm (*115*).
- Price of lenalidomide was increased three times over the course of 2017 with a cumulative percentage increase of 19.8% (*116*). The manufacturer noted that "pricing decisions reflect the benefits that our innovative therapies provide to patients, the healthcare system and society" and the value of lenalidomide "continue to increase, supported by the growing clinical and real-world outcomes for patients in the approved indications" (*116*). However, the manufacturer did not provide evidence to support how the benefits have changed in such a short period of time.

Pharmaceutical companies typically undertake extensive planning activities for developing pricing and market access strategies many years before the clinical evidence from the pivotal Phase III trials become available (i.e. before the main component of the so-called value is known). These activities invariably involve extensive consultations with business consultants, expert clinicians and payers. Fig. 3.2 shows a summary of activities relating to the price planning of palbociclib – a medicine used for the treatment of breast cancer (*112*). The manufacturer of palbociclib developed its pricing strategy largely based on price benchmarking with other cancer medicines, some of which were not comparable clinically. The manufacturer also engaged consultants to determine, and possibly influence, clinicians and health plan officials' potential willingness to pay for the so-called value of the medicine.

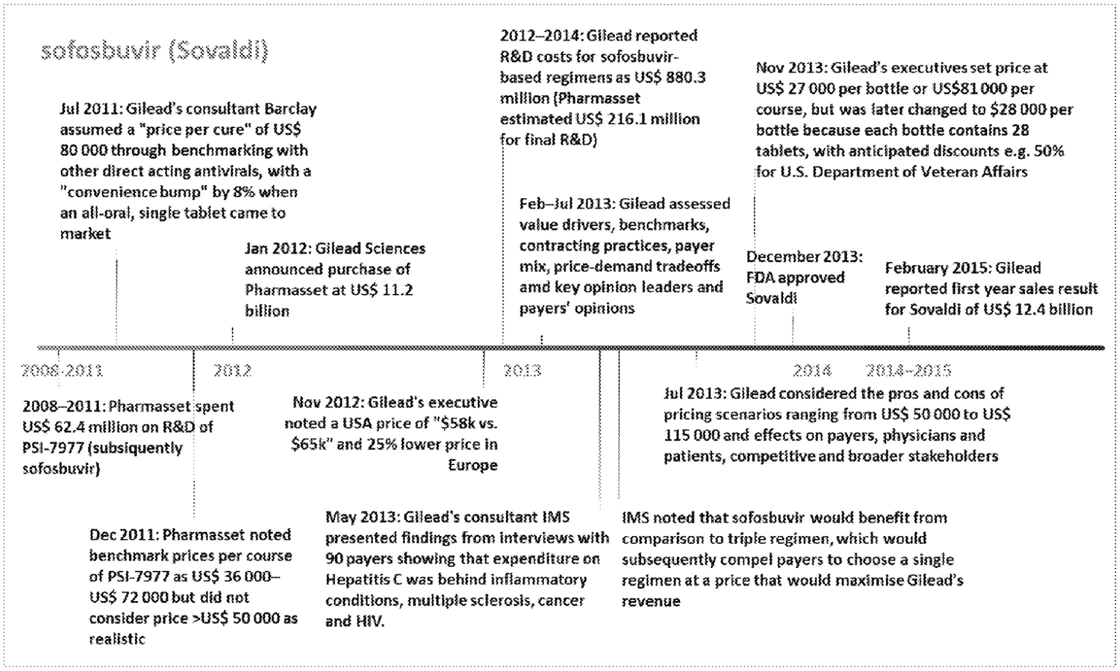
Fig. 3.2: Timeline of price planning activities for palbociclib


palbociclib (Ibrance)
Dec 2009: Phase II clinical trial commenced
Nov 2011: Review of early clinical trial data to inform commercial decision for further clincial trials
Interviews with 125 clinicians in six cities to share clinical evidence and to consider (and possibly influence) comparable treatments to which Ibrance's price would be pegged: Kadcyla, Perjeta and Afinitor which had prices between US$9 000 and US$12 000
Day-long mock-interviews with health plan officials to understand the acceptability of pricing and reimbursement requirements
Assessing potential prescription numbers and revenue at prices between US$9 000 and US$12 000
Feb 2015: US FDA approved Ibrance for the treatment of postmenopausal women with estrogen receptor-positive, HER2-negative metastatic breast cancer with no prior endocrine-based therapy
2011
2012
2013
2014
2015
Pharmaceutical firm commenced market analysis
Oct 2013: Phase III trial commenced
Dec 2012: Results from Phase II clinical trial was reviewed
Survey >80 health plan officials to understand any restrictions they might put on for medicine monthly prices US$9 000-$12 000
Jan 2015: Seeking approval for the final price (US$9 850) with final consideration to the benchmark price of Afinitor (US$10 537)

Source: Author's visualization based on information presented by Rockoff (*112*)

A further example is the pricing of sofosbuvir (Sovaldi) – a medicine used for the treatment of hepatitis C virus infection, potentially preventing future cases of liver cancer. Fig. 3.3 (p.23) shows the timeline of price planning for Sovaldi based on information presented in the report by the Committee on Finance of the United States Senate (*100*). In this case, it shows the evolution of the expected price of Sovaldi from prior to its acquisition (<US$ 50 000 per course) to the final launch price of US$ 84 000 per course. The final price was decided based on an anticipated rise in revenue even though the manufacturer expected the number of patients receiving the medicine would decline (p.43) (*100*), and various stakeholders would react negatively to the firm's final pricing of the product. Furthermore, the manufacturer set a high price for Sovaldi with a view to consolidate the market's price expectation in preparation for setting an even higher price for a combination product that contains sofosbuvir (Harvoni) that would be launched after Sovaldi. It also included an arbitrary price increase from US$ 27 000 per bottle to US$ 28 000 per bottle (i.e. 3.7% increase) because it would "be easy from the press release, from 28 days and $28,000" (p.57) (*100*). This example demonstrates that pricing solely according to commercial goals will impair a health system's ability to achieve public health goals because high prices limit patient access, thereby limiting the full value potential of the innovation.

Fig. 3.3: Timeline of price planning activities for sofosbuvir



Jul 2011: Gilead's consultant Barclay assumed a "price per cure" of US$ 80 000 through benchmarking with other direct acting antivirals, with a "convenience bump" by 8% when an all-oral, single tablet came to market

Jan 2012: Gilead Sciences announced purchase of Pharmasset at US$ 11.2 billion

2012–2014: Gilead reported R&D costs for sofosbuvir-based regimens as US$ 880.3 million (Pharmasset estimated US$ 216.1 million for final R&D)

Feb–Jul 2013: Gilead assessed value drivers, benchmarks, contracting practices, payer mix, price-demand tradeoffs amd key opinion leaders and payers' opinions

Nov 2013: Gilead's executives set price at US$ 27 000 per bottle or US$81 000 per course, but was later changed to $28 000 per bottle because each bottle contains 28 tablets, with anticipated discounts e.g. 50% for U.S. Department of Veteran Affairs

December 2013: FDA approved Sovaldi

February 2015: Gilead reported first year sales result for Sovaldi of US$ 12.4 billion

2008–2011: Pharmasset spent US$ 62.4 million on R&D of PSI-7977 (subsiquently sofosbuvir)

Nov 2012: Gilead's executive noted a USA price of "$58k vs. $65k" and 25% lower price in Europe

Jul 2013: Gilead considered the pros and cons of pricing scenarios ranging from US$ 50 000 to US$ 115 000 and effects on payers, physicians and patients, competitive and broader stakeholders

Dec 2011: Pharmasset noted benchmark prices per course of PSI-7977 as US$ 36 000–US$ 72 000 but did not consider price >US$ 50 000 as realistic

May 2013: Gilead's consultant IMS presented findings from interviews with 90 payers showing that expenditure on Hepatitis C was behind inflammatory conditions, multiple sclerosis, cancer and HIV.

IMS noted that sofosbuvir would benefit from comparison to triple regimen, which would subsequently compel payers to choose a single regimen at a price that would maximise Gilead's revenue

Source: The staff of Ranking Member Ron Wyden and Committee Member Charles Grassley (*100*) in the United States Senate

3.2.1.5 Financial returns to incentivize investment in R&D

The industry also often justifies prices of medicine by stating that return on investment needs to be sufficient to incentivize the discovery of future medicines (*109*). To this point, the industry noted that 20% of its revenues were re-invested into R&D (*87*).

There are debates about whether the returns generated from the sales of medicines, including cancer medicines, are sufficient for pharmaceutical companies to cover their past R&D expenses, maintain their operations and engage in future drug discovery research. For example, some commentators have observed that the revenue generated from the sales of imatinib had exceeded the costs of R&D within two years and "the revenues over the subsequent years of the patent would represent generous profits to the company" (*30*). Another study found that total revenue from the sales of 10 cancer medicines since approval over a median of four years (US$ 67.0 billion) was 9.3 times the total R&D spending of US$ 7.2 billion (or 7.4 times using an estimated risk-adjusted R&D costs of US$ 9.1 billion) (*94*).

To systematically assess the financial return of cancer medicines, this report undertook a study to quantify the reported global incomes from the sales of individual medicines approved by the US FDA in 1989–2017 for the treatment of haematological cancers, solid tumours and related conditions such as neutropenia and hypercalcaemia (*117*). Itemized product sales data were extracted from the consolidated financial reports of originator companies, supplemented and verified with publicly available sources where necessary. Sales incomes were reported net of rebates and discounts but without accounting for expenses and taxes, as per *International Financial Reporting Standards*.

Of the 156 US FDA-approved cancer medicines identified, 99 had data for more than half of the years since approval and were included in the analysis. Total sales from this set of medicines (US$ 106.9 billion) represent 80.4% of the estimated global revenue of cancer medicines in 2017 (US$ 133 billion) (*18*).

The analysis found that as at the end of 2017, forty-nine (49.5%) of the cancer drugs had cumulative sales of over US$ 5.0 billion. At the end of 2017, five drugs had accrued sales incomes of greater than US$ 50 billion for the originator companies: rituximab (US$93.7 billion), trastuzumab (US$ 88.2 billion), bevacizumab (US$ 83.4 billion), pegfilgrastim (US$ 64.0 billion), imatinib (US$ 63.8 billion) (Fig. 3.5, p.26). The cumulative sales of some drugs appeared to be lower than the overall set of drugs: ziv-aflibercept, belinostat, degarelix, ibritumomab tiuxetan, ofatumumab and romidepsin. However, the financial returns for some of these medicines might have been fully recovered. For example, the R&D of belinostat received substantial contributions from public sector funds (*118,119*). The income for ibritumomab tiuxetan is likely to be underestimated because it only included sales in the USA but not the historical sales in Europe by (the now defunct) Schering AG. For ofatumumab, the sales trajectory might have been affected by the introduction of alternative drug for chronic lymphocytic leukemia in 2014 (i.e. ibrutinib), transfer of marketing right from GlaxoSmithKline to Novartis in 2014, as well as possible strategic transitioning the drug for use in multiple sclerosis (*120*).

Many cancer medicines were also found to have generated substantial financial returns for the originator companies even after loss of market exclusivity, particularly for biologics (Fig. 3.5, p.26). For example, the principal patents on filgrastim expired in August 2006 (Europe) and December 2013 (USA) following its launch in 1991 (*121*). Although its income has declined following competition from biosimilar products, filgrastim continued to generate more than US$ 500 million annually (range: US$ 549.0 billion–1.2 billion) for the initial originator company after losing market exclusivity in 2014. The originator company of filgrastim also reported more than US$ 4 billion in sales income annually from pegfilgrastim, whose principal patents expired in October 2015 (USA) and August 2017 (Europe) (*121*). The reported annual sales incomes for anastrozole, bicalutamide, rituximab, trastuzumab, capecitabine, temozolomide and thalidomide were also in the hundreds of millions of US dollars for the originator companies following expiry of their principal patents.

> *Many cancer medicines have generated substantial financial returns for the originator companies after loss of market exclusivity*

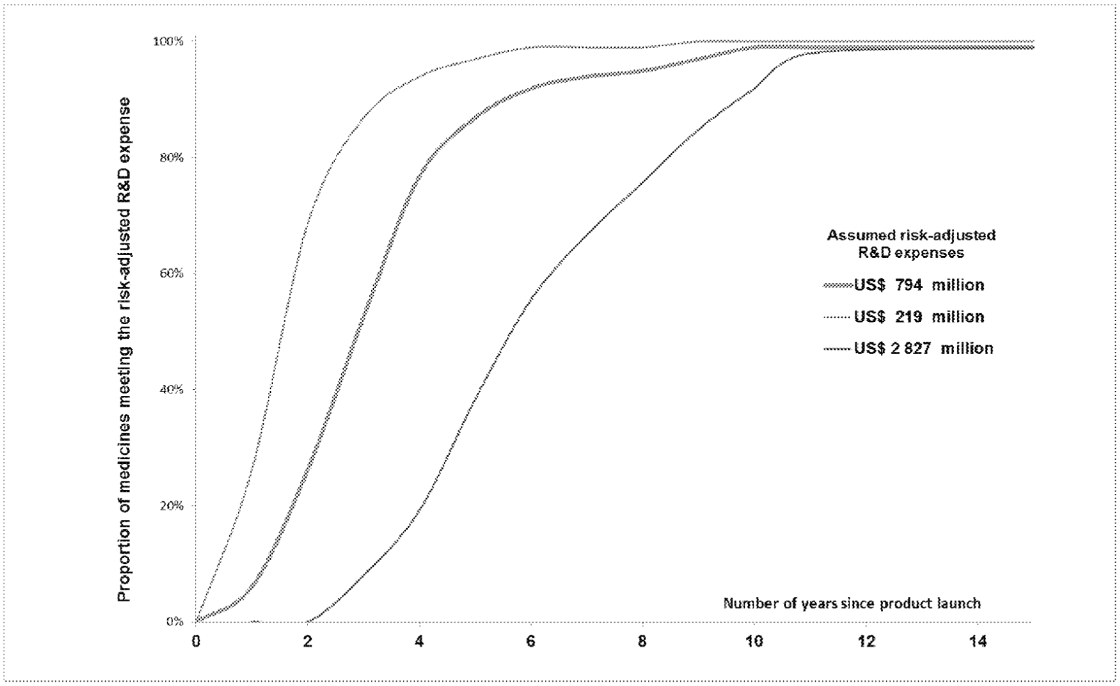
The analysis suggests that the sales revenues of a majority of cancer medicines are significantly above the risk-adjusted costs of R&D estimated in the literature. As shown in Fig. 3.5, as at the end of 2017, the cumulative sales of 73 (74.5%) and 56 (57.1%) cancer medicines since launch were above the assumed median risk-adjusted R&D costs of US$ 794 million and the upper threshold of US$ 2.8 billion, respectively. In total, 99 cancer medicines generated US$ 1 216.7 billion in cumulative incomes between 1989 and 2017, representing an average return of US$ 14.50 in sales income (range: US$ 3.30–55.10) for every dollar invested for R&D, assuming a risk-adjusted R&D cost of US$ 794 million (range: US$ 2 827 million; US$ 219 million) (*94*). The returns from this set of medicines will continue to rise because many molecules have long remaining periods of market exclusivity (e.g. ibrutinib, nivolumab, palbociclib, pembrolizumab). When the R&D costs for cancer drugs were assumed to be twice as high as the base-case estimates (i.e. US$1 588 million, range: $438 million, $5 654 million), the average income return was US$6.70 (range: US$1.20; US$27.10) per dollar invested for R&D. Finally, another sensitivity analysis incorporating the full R&D costs but zero sales incomes for the 57

> *By the end of 2017, the average income return from the 98 cancer medicines for the originator companies was US$ 14.50 (range: US$ 3.30–55.10) for every risk-adjusted dollar of R&D spending*

drugs excluded in the base-case analysis showed that the overall income return per R&D dollar remained high at US$8.80 per R&D dollar (range: US$1.70; US$34.40).

The median time to generate revenue to fully cover risk-adjusted R&D cost of US$794 million was 3 years (range: 2 years; 5 years, n=73). For the maximum estimated risk-adjusted cost of R&D (US$2 827million), the time to cost recovery was 5 years (range: 2 years; 10 years, n=56). A threshold analysis found that 99% of the 45 cancer drugs with sales data 10 years from their first year of launch had generated incomes sufficient to at least offset the risk-adjusted R&D costs irrespective of the assumed threshold values for R&D costs. A threshold analysis found that 99% of the 45 cancer medicines with sales data for 10 years from their first year of launch had generated incomes sufficient to at least offset the risk-adjusted R&D costs irrespective of the assumed threshold values for R&D costs (Fig. 3.4).

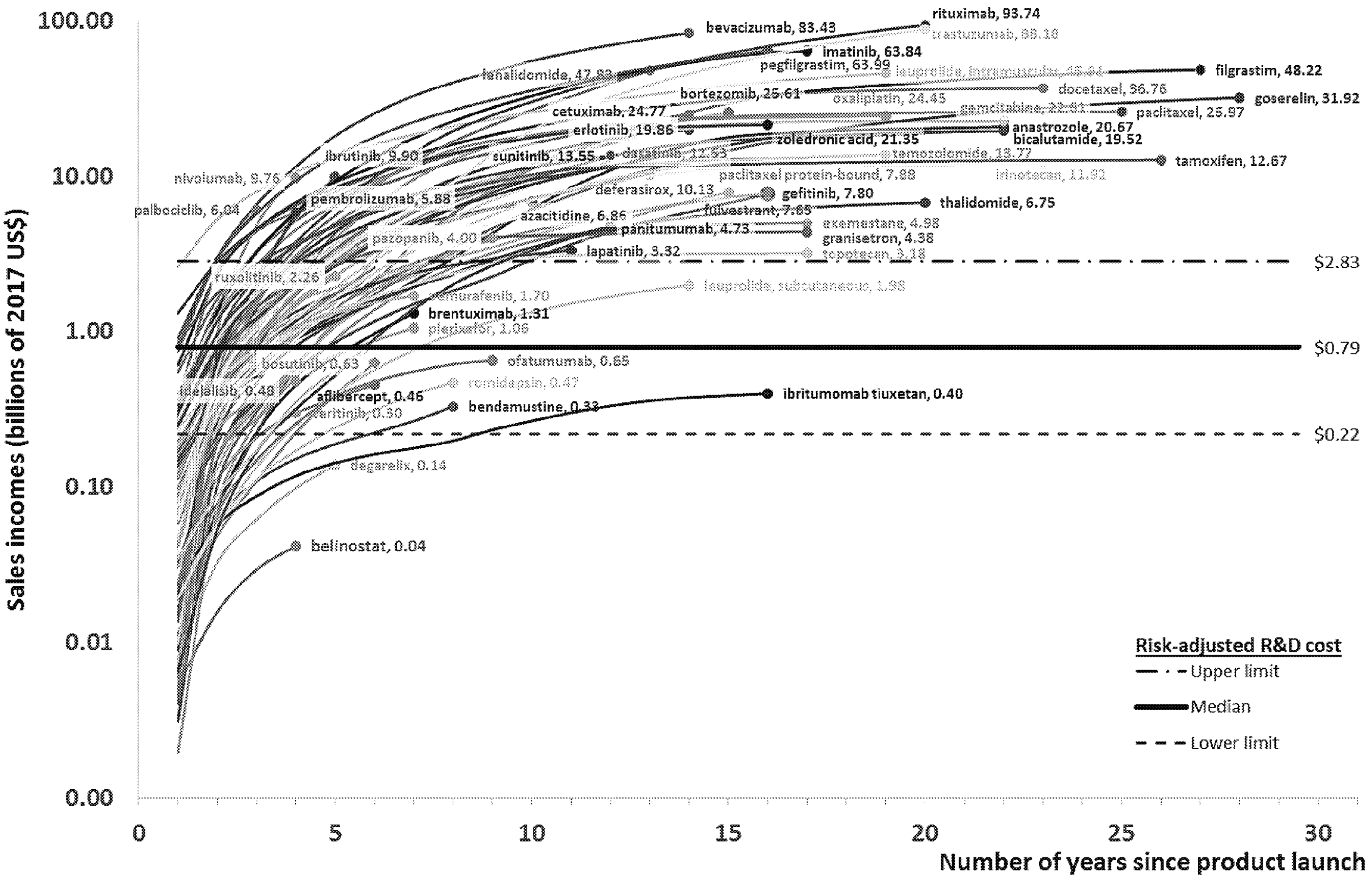
Fig. 3.4: Threshold analysis of revenue return, by R&D expenses and years since product launch



Source: Author's analysis based on sales figures of products from 1989–2017 presented in companies' annual reports and public reports (*117*)

In summary, cancer medicines, through high prices, have generated returns for the originator companies far in excess of the R&D costs and financial rewards to finance and incentivize future R&D. Section 4.4 will discuss how excessive returns could distort investment, encourage rent-seeking and stifle innovation.

Fig. 3.5: Cumulative sales incomes of cancer medicines in 2017 US dollars, by molecule



Source: Author's analysis based on sales figures of products from 1989–2017 presented in companies' annual reports and public reports (*117*)

KEY POINTS

- **Relationship between inputs throughout value chain and price setting:** The pharmaceutical industry and various commentators have noted four determinants of medicine prices: (1) costs of R&D; (2) costs of production and commercialization; (3) value of medicine; and (4) sufficient returns for future R&D. Achieving commercial goals is clearly another determinant.
- **Estimates of medicine R&D costs are highly variable and not transparent:** Irrespective of the true magnitude of R&D costs (estimated as between US$ 200 million and US$ 2 800 million), current prices of (and profits from) cancer medicines are at least sufficient to account for, if not in excess of, the risks inherent in the R&D of cancer medicines.
- **The costs of R&D and production may bear little or no relationship to how pharmaceutical companies set prices of cancer medicines**. Instead, pharmaceutical companies set prices according to demand-side factors, with a focus on extracting the payers' maximum willingness or ability to pay for a medicine.
- **Value of medicines:** Adoption of value-based pricing has not established medicine prices reliably because of various sources of uncertainties: variable robustness of value assessment system, incomplete evidence to inform value, straw man comparisons, different conceptualization and perception of values. Case studies indicate that pharmaceutical companies have set prices based on commercial goals, rather than aiming to realize the full value potential of cancer medicines through improved access.
- **Returns on investment**: Current returns from many cancer medicines are likely to be in excess of the factors of production required for maintaining operation and incentivizing ongoing R&D. As at 2017, a set of 99 cancer medicines returns US$ 14.50 in sales income (range: US$ 3.30–55.10) for every dollar invested.

3.2.2 Understanding medicine pricing through market structure

This section takes a macro-level view of the cancer medicines sector, with a view to explaining some of the pricing approaches and behaviours used by pharmaceutical companies.

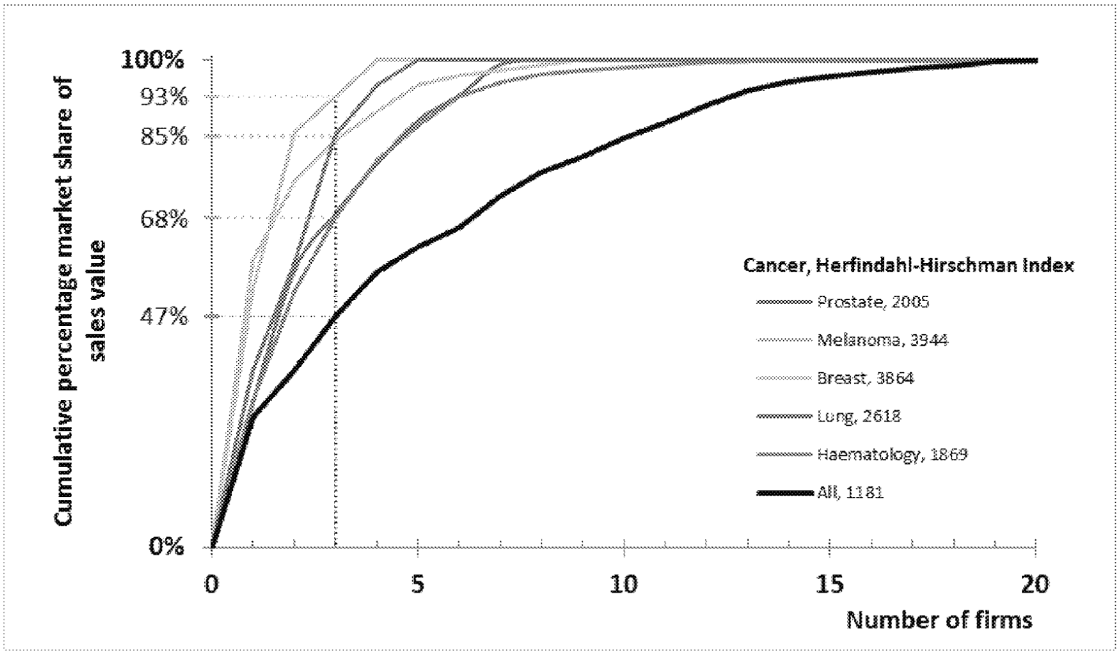
3.2.2.1 Market structure for cancer medicines

The market structure of cancer medicines is characterized by imperfect competition, with evidence of individual companies holding monopoly over specific cancer therapeutic areas. To understand the level of market concentration in the cancer medicines market, the market share of cancer medicines in 2017 by cancer type was assessed. The Herfindahl-Hirschman Index (HHI) (*122*) – a measure of market concentration – was also calculated by summing the squared values of the market share of each company competing in the cancer area. A higher HHI value indicates a market being closer to monopoly, and if there were only one firm in the market HHI would be 10 000.

> *Three companies accounted for about half of the global market of cancer medicines by 2017 sales value*

The analysis found that three companies accounted for about 50% of the global market of cancer medicines by 2017 sales value (Fig. 3.6). The market is considered highly concentrated in certain cancer therapeutic areas. For example, three companies – Bristol-Myers Squibb, Ono Pharmaceutical and Merck & Co – accounted for nearly 97% of the 2017 global market for the melanoma medicines. This is confirmed by a HHI of 3 944 points, which exceeded the United States Department of Justice and the Federal Trade Commission's threshold value of 2500 points for a "highly concentrated market" (*122*). The level of market concentration would be even higher if the analysis were to consider the existing collaboration between Bristol-Myers Squibb and Ono Pharmaceutical for developing and commercializing nivolumab and ipilimumab (*123*). The analysis also found a highly concentrated market for breast cancer, and moderately concentrated markets for prostate, lung and haematological cancers (Fig. 3.6). Companies with market dominance are termed price makers because they are able to set higher prices for their medicines while maintaining market share.

Fig. 3.6: Distribution of market share by 2017 sales value and Herfindahl-Hirschman Index



Source: Author's calculation based on 2017 sales figures of products presented in companies' annual reports

3.2.2.2 Sources of market dominance

There are at least four sources of market dominance in the pharmaceutical sector for cancer medicines.

Firstly, like other new medicines, protection of intellectual property keeps generic or biosimilar competition out of the market for varying periods of time depending on the jurisdictions. Relevant intellectual property includes patents on new molecules, new combinations, variations of existing molecules, and patents on minor variations of an existing product aiming at consolidating an existing market position. In many developed countries, pharmaceutical companies benefit from additional (market) exclusivity periods that delay entry of competitor products, in particular the application of data exclusivity to protect the investment in the clinical trials data submitted to regulatory authorities (*124*). This means that other companies cannot rely on this set of data to obtain market approval without the consent from the originator firm during the exclusive period. In particular to protect the market position of their blockbuster drugs, companies may adopt a variety of strategies to preserve their market position through launching new combination formulations, filing patents over new features such as coating, salt moiety and method of administration, to name a few (*125,126*). In the United States, the combined effect of these instruments and strategies creates actual market exclusivity for 12–16 years (*127*).

Secondly, medicines belonging to the same therapeutic class may not be readily substitutable clinically because of differences in disease characteristics, therapeutic and safety profile, and standard evidence-based treatment protocols. For example, guidelines suggest the use of crizotinib as the first-line treatment for advanced non-small cell lung cancer with ALK translocation, but current evidence only recommends the use of other ALK inhibitors (ceritinib and alectinib) upon disease progression following crizotinib treatment (*128*). For this reason, crizotinib holds monopoly as the first-line treatment in this patient population.

Thirdly, pharmaceutical companies may pursue what is called differentiated oligopoly, by occupying a particular segment of the market even though the medicines may be considered interchangeable therapeutically. For example, nivolumab and pembrolizumab are two monoclonal antibodies targeting programmed death (PD-1) for the treatment of metastatic non-small cell lung cancer with comparable therapeutic effects (*129*). However, the regulatory approved use of pembrolizumab requires confirmation of PD-L1 expression based on approved test, while the use of nivolumab does not require such confirmation even though PD-L1 expression has prognostic value for both treatments. On the other hand, pembrolizumab has a dosing schedule of every 3 weeks while nivolumab has a dosing schedule at every 2 weeks (*129*). Based on these characteristics, the companies may engage in non-price competition (e.g. through promotion) to distinguish these attributes for gaining dominance in a specific market segment.

Finally, potential competing companies may not be able to enter the market easily upon conclusion of the market exclusive period for the originator company. The barriers to entry are particularly high for the entry of biosimilar products due to a range of factors (*130,131*). This is particularly pertinent for cancer medicines because about 2 in 5 of them are biological products. Some of the documented examples of barriers to uptake of cancer medicines include the following.

- **Manufacturing and quality assurance processes are more complex and of higher cost**: Cell-based production processes are less predictable than chemical processes, leading to potential quality assurance issues e.g. the production of L-asparaginase (*132*).
- **Different regulatory requirements**: While there is a trend towards international harmonization of regulatory requirements for biosimilar products (*133,134*), varying rules regarding nomenclature and substitution in some jurisdictions may create barriers for the introduction of these products and impair competition (*135*).
- **Patent disputes and extension of exclusive marketing rights:** Originator companies may initiate patent disputes with the first biosimilar competitor, which may discourage or delay its market entry. Examples of patent disputes include filgrastim (*136*), trastuzumab (*136*) and rituximab (*137*).
- **Competition-limiting demand-side factors:** There are discrepancies in prescribing and dispensing requirements across jurisdictions regarding interchangeability of biosimilar products, reflecting in part the differences in position about the safety of switching between biologics and their biosimilar analogues (*138*). Furthermore, clinicians and patients may have different levels of awareness and attitudes about biosimilar products (*139–141*). These factors may lower demand for biosimilar products, thereby limiting competition and enhancing the market dominance for the originator.

3.2.2.3 Pricing strategies of a monopolist

While recognizing the limitations of economic theories in precisely explaining all real-world observations, known principles of economic theory can, in general terms, clarify some of the pricing strategies of pharmaceutical companies that hold monopoly on certain medicines, briefly described below.

> Economic theory suggests that monopolies are inefficient because monopolists would overcharge, under-produce and produce at higher costs than a competitive market.

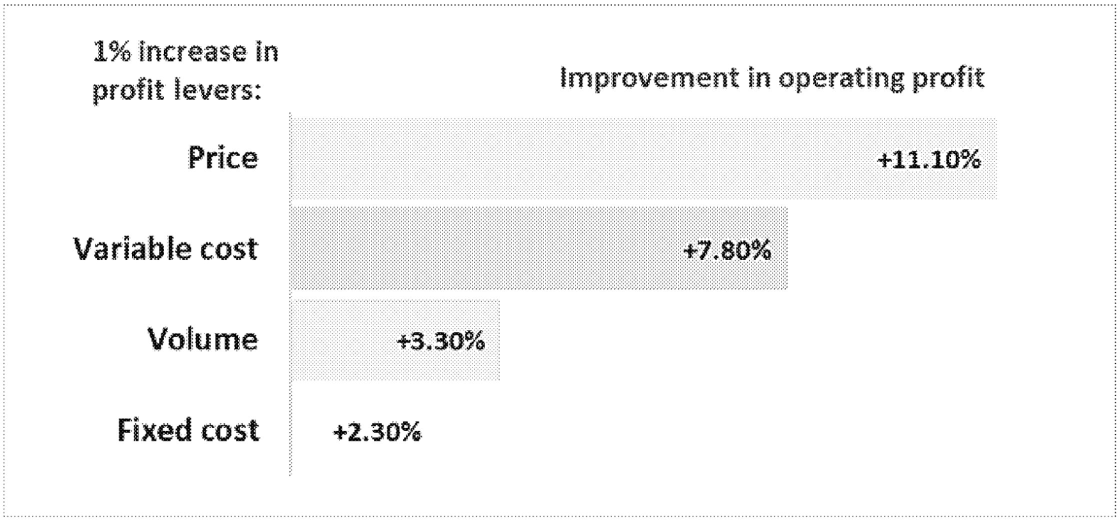
Economic theory suggests that a monopolist would dictate prices of their products as a price maker because there are no close substitutes. Economic theory also indicates that to maximize its profit a monopolist would supply at a quantity lower and at higher price than what would maximize societal welfare. This would cause a transfer of welfare from consumers to the monopolist, as well as a loss of overall economic efficiency for the society (i.e. deadweight loss). Furthermore, at this quantity, the production is not at the lowest average total cost, in contrast to the expected production in a competitive market. This means that it is not "productively efficient" in economic lexicon. In summary, economic theory suggests that monopolies are inefficient because monopolists would overcharge, under-produce and produce at higher costs than a competitive market.

Furthermore, a monopolist might use its market dominance to charge different prices for the same product to different consumers – a pricing approach known as price discrimination. This would allow the monopolist to maximize its profit according to the consumers' price elasticity of demand, that is the consumers' sensitivity to choosing whether to buy a product in response to the changing product price according to their willingness and ability to pay for that product. In simple terms, the monopolist would sell the product at higher prices to those consumers who value the product higher and are willing, or able, to pay more for it at that price. The monopolist would undertake price discrimination for different markets insofar as there are barriers in place to prevent the consumers in various markets from taking advantage of the differences in price and make a profit from it (i.e. arbitrage). As the medicine market often depends on the health systems or patients' ability to pay, the market outcomes would often not meet public expectations as well as public health objectives. Finally, monopolies may impair innovation because there is no incentive to innovate in the absence of competitors.

In the context of cancer medicines, there are ample examples where the pharmaceutical companies holding monopolies have set high prices to maximize their profits (*142*). Given the pricing power of monopolies, there is also a tendency for companies to adopt what is known in marketing lexicon as the "market-skimming pricing" for cancer medicines, where they would initially set a price as high as the market would bear, with a view to subsequently reducing the price over time to "skim the cream" from customers with lower willingness to pay. High prices often result in restricted access (i.e. lower quantity). This is because health systems or patients do not have the capacity to pay for the medicines at prices higher than their ability to pay (*143*), even in high-income countries (*144–146*). The problem of unaffordable prices of cancer medicines is particularly prominent in markets where prices are less regulated (*147*) or during global financial crisis (*148*). Furthermore, like a monopolist, pharmaceutical companies often adopt price discrimination as described previously, but refer to it as "tiered or differential pricing" (*149*). While it is probable that differential pricing might enhance affordability and accessibility, prices are frequently kept undisclosed under such arrangements (so as to prevent arbitrage and consumers referring to lower prices). This makes markets less transparent because it is unknown how "differential" the prices actually are and whether differential pricing had actually improved access to affordable medicines. This informational asymmetry is a known condition for causing market failure.

It is also worth noting that pharmaceutical companies' focus is invariably on increasing price rather than other factors of profit, such as increasing volume or reducing costs. There are at least two reasons for explaining this behaviour. Firstly, as indicated by a widely-cited study by a global consulting firm, increasing price would generate larger improvement in profit than other levers of profit (Fig. 3.7, p.31) (*150*). This may have influenced repeated price increases noted in the market for cancer medicines (*147,151*) and indeed, markets for patented and generic medicines in other therapeutic areas (*152–154*). Secondly, as there are many factors influencing demand of medicines other than price (*50*), it would be sensible for companies focused solely on maximizing profits to focus on price because as it has been said "price is certainty and volume is a bet".

Fig. 3.7: Comparison of factors of profit



Source: Exhibit 1 in Marn and Rosiello (*150*) (Reproduced with permission)

KEY POINTS

- **Market concentration**: The market structure of cancer medicines is characterized by imperfect competition, with evidence of individual companies holding monopoly over specific cancer therapeutic areas. Companies with market dominance are called price makers because they are able to set higher prices while maintaining market share.
- **Sources of market dominance**: (1) Protection of intellectual property allows companies to prevent generic/biosimilar competition and to employ various strategies to preserve their market position; (2) lack of clinical substitutes occurs because of the differences in disease characteristics, therapeutic and safety profile, and standard evidence-based treatment protocols; (3) presence of "differentiated oligopoly" occurs, where companies attempt to differentiate similar products; and (4) entry barriers prevent other companies from entering the market due to factors such as regulatory requirements, manufacturing requirements, patent disputes, and demand-side factors (interchangeability criteria, perceived inferiority).
- **Monopolies are inefficient** because monopolists would overcharge, under-produce and produce at higher costs than in a competitive market, as evident in the cancer medicine market.
- **Companies focus on price** because increasing price may generate larger improvement in profit than other levers, and uptake of cancer medicines is uncertain because of other non-price-related barriers to access.

3.3 Payers' pricing approaches

Government or institutional authorities responsible for determining and managing prices of medicines have used various pricing approaches across the supply chain and at various time-points throughout the product life-cycle. This section provides a short summary of these approaches with examples on the pricing of cancer medicines where applicable. Interested readers may consult resources listed in Appendix D for detailed and context-specific information on various pricing approaches.

3.3.1 Setting medicine prices

3.3.1.1 Cost-based pricing

Cost-based pricing is also known as cost-plus pricing. As its name implies, this pricing approach considers the costs associated with the inputs required for the production of goods or services, such as cancer medicines and their administration. This pricing approach requires cost information within the predefined scope along the value chain to the point at which the price would be set. For example, if cost-based pricing were to be used for determining the ex-manufacturer price of a medicine, it would require information regarding direct material costs, direct labour costs, overhead costs associated with R&D, manufacturing, regulatory processes and compliance, and other costs of business operation. To determine the final price, the manufacturer and the pricing authority would need to come to an agreement on profit margin additional to the estimated costs, based on a mutually-acceptable level and structure (i.e. percentage or a fixed amount).

Cost-based pricing has not been widely used in the pharmaceutical sector for setting medicine prices at the ex-manufacturer or ex-wholesaler levels. This report identified three countries where cost-based pricing has been noted for setting ex-manufacturer prices (Table 3.1), although the extent of use in practice and the practical details are not in the public domain.

Table 3.1: Examples of cost-based pricing, by jurisdiction

Jurisdiction	Medicine type	Price determination method
Australia *(155)*	Stand-alone product where there is no comparator (i.e. benchmark)	Price is calculated as the sum of the following components. • Costs of manufacturing: o materials: active content, packaging, other materials o labour and quality assurance o other costs: e.g. equipment, depreciation, manufacturing overhead. • Other costs: product finance, pre-distribution warehousing, regulatory fees and charges. • A mark-up of around 30%, but may vary on a case-by-case basis.

Jurisdiction	**Medicine type**	**Price determination method**
Japan (*156*)	New drugs without an existing reference drug	Price is the sum of the following components. • Manufacturing (importation) costs: o raw materials: active ingredients, additives, containers and packaging, etc.) o labour: average labour costs x time o manufacturing cost. • Costs of sales and general administration, R&D: (45.9%). • Operating profit: industry average percentage of revenue (14.6%) with ±50% adjustment based on novelty, efficacy and safety compared to existing drugs. • Distribution costs: industry average percentage of revenue (0.7%). • Consumption tax (8%).
United Kingdom (*157,158*)	All branded medicines from companies participating in the Pharmaceutical Price Regulation Scheme	**Indirect** regulation on price through a voluntary scheme that regulates profit on the basis of a range of maximum allowances for the following cost components: • R&D, manufacturing costs, costs for information provision including statutory information requirements, costs for promotion (sales, marketing) and costs for general administration. • The scheme set a target rate of return on capital of 21% and a return on sales of 6%, with a margin of tolerance (i.e. profit) threshold of 50%.

Source: Australia (155), Japan (156), the United Kingdom (157,158)

The infrequent use of cost-based pricing is in part because of the practical challenges in obtaining reliable cost information (*159*) and implementing such a pricing approach. Firstly, the global nature of pharmaceutical companies and the complexity of their cost structures make it difficult to allocate the costs specific to the setting of prices (*42,160*). Furthermore, some commentators also considered that any regulation on profit margin based on the costs of production may result in weak incentives for the pharmaceutical sector to innovate (*160*). Secondly, a cost-based pricing structure may in fact provide perverse incentives for the companies to undertake R&D and production inefficiently (*42*) so that the product would achieve a higher price, and a higher profit margin if a percentage mark-up structure were in place. Finally, if a firm holds monopoly over a medicine, economic theory suggests that setting the medicine price equal to marginal cost of production with insufficient profit margin might result in the monopolist taking a loss because marginal cost is below the average total cost of production. If this were to happen, the monopolist would exit the market and cause medicine shortages.

Cost-based pricing is infrequently used because of the practical challenges in obtaining reliable cost information

Notwithstanding, cost-based pricing has been used much more widely to determine prices downstream in the value chain (i.e. ex-pharmacy and consumer prices) because the cost of goods is easier to determine. For example, many countries set consumer or reimbursable prices of medicines by ascertaining the cost of medicines (e.g. wholesaler price), applying a pre-agreed percentage or fixed amount of mark-up, and adding any costs associated with provision of service (e.g. dispensing, storage, preparation of chemotherapy infusion). The structure of mark-ups is discussed further in Section 0.

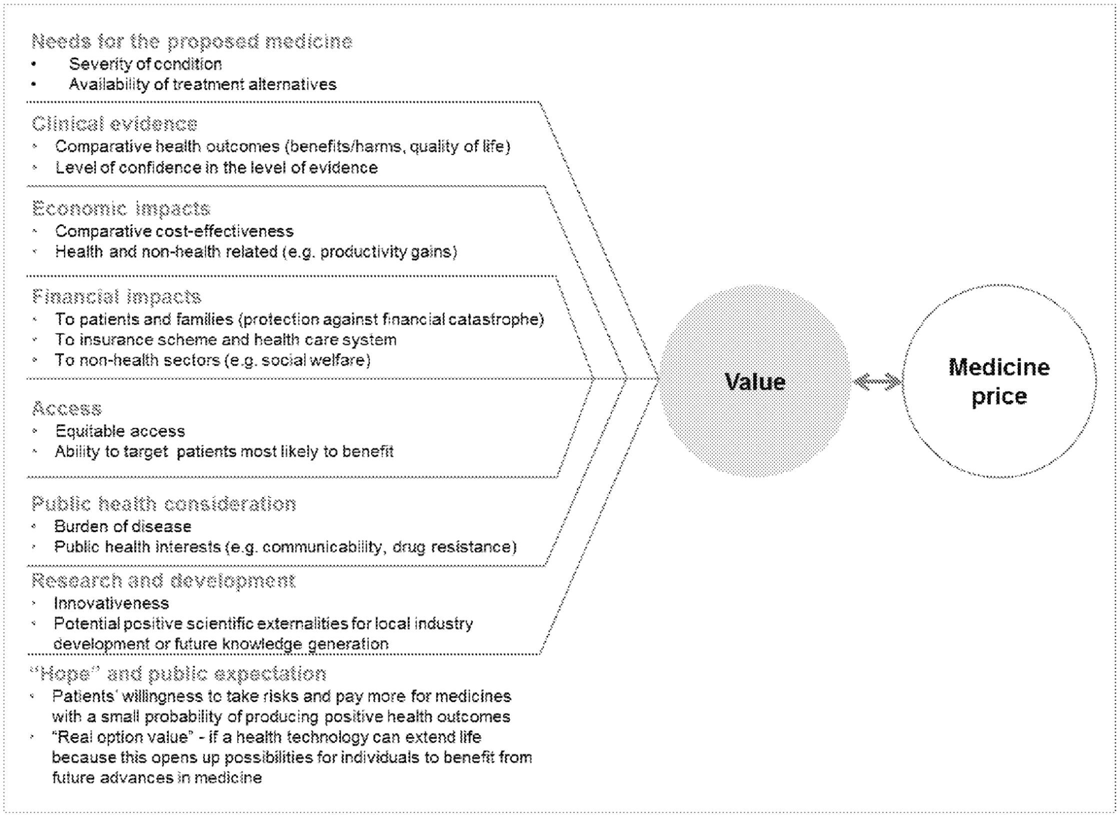
3.3.1.2 Value-based pricing

Value-based pricing or value pricing aims to determine the prices of medicines according to the value or worth that patients and health systems attribute to the medicines. In theory, by linking price to value, value-based approaches are more likely to encourage companies to innovate and produce medicines with attributes that society and governments value most. In the context of medicines this would mean the public and government would be willing to pay for medicines that improve health conditions and minimize harms.

As discussed in Section 3.2.1.3 (p.20), many countries have adopted *elements* of value-based pricing in informing the prices of medicines, but there remains considerable challenge in assessing, measuring and translating the value of a medicine to a price. In particular, there is no universally accepted view on what dimensions of value should be considered for the purpose of determining medicine prices. Fig. 3.8 (p.34) shows the various dimensions of value noted in the literature and government guidelines, summarized into eight themes. Common dimensions considered in health technology assessments are: clinical and public health needs for the proposed medicine, clinical evidence, economic and financial impacts, access to medicines and public health considerations. More debatable is whether to include value related to R&D of medicines such as innovativeness of the medicine, and the need to incentivize future R&D through higher prices.

> *Many countries have adopted elements of value-based pricing to inform medicine pricing, but measuring the so-called value of a medicine and translating it to a price are difficult*

Fig. 3.8: Dimensions that may be considered for determining the value of medicines


Needs for the proposed medicine
Severity of condition
Availability of treatment alternatives
Clinical evidence
Comparative health outcomes (benefits/harms, quality of life)
Level of confidence in the level of evidence
Economic impacts
Comparative cost-effectiveness
Health and non-health related (e.g. productivity gains)
Financial impacts
To patients and families (protection against financial catastrophe)
To insurance scheme and health care system
To non-health sectors (e.g. social welfare)
Access
Equitable access
Ability to target patients most likely to benefit
Public health consideration
Burden of disease
Public health interests (e.g. communicability, drug resistance)
Research and development
Innovativeness
Potential positive scientific externalities for local industry development or future knowledge generation
"Hope" and public expectation
Patients' willingness to take risks and pay more for medicines with a small probability of producing positive health outcomes
"Real option value" - if a health technology can extend life because this opens up possibilities for individuals to benefit from future advances in medicine
Value
Medicine price

Source: (110,111,156,161,162)

Even within a clearly defined set of value dimensions, the measurement and enumeration of individual dimensions to medicine prices may be subject to considerable levels of uncertainties. Firstly, as discussed in Chapter 2, many cancer medicines only have evidence on improvements in surrogate end-points that are poorly correlated with patients overall survival and quality of life at the time of regulatory approval (*62,64,65,68*). Secondly, medicines may have varying levels of value (e.g. magnitude of benefits) for different indications and patient populations. For example, EGFR tyrosine kinase inhibitors, including erlotinib, are recommended as the preferred first- and second-line treatment in patients with EGFR-mutated non-small-cell lung cancer because of evidence showing clinically meaningful response rates and improvement in quality of life (*163*). In contrast, even though erlotinib was approved for use as the first-line treatment for patients with advanced pancreatic cancer in combination with gemcitabine, the improvement in median survival was only 12 days compared with gemcitabine alone (6.24 months vs 5.91 months) in the pivotal randomized trial (*75*). The differences in value therefore pose challenges in determining the market price. Thirdly, some dimensions are not readily quantifiable and require a certain level of judgement or negotiation to inform pricing. For example, if innovativeness of a medicine were considered within scope, determining the level of innovativeness of a medicine and the magnitude of price premium to be added would require judgement (e.g. pricing in Japan (*156*)).

At a system level, implementing health technology assessment to determine value and price is complex. A well-developed system for such undertakings requires not only strong capability for performing appraisals and technical analyses, but also requires a highly supportive politico-legal environment to support the decision-making process, strong health information system, integrated service delivery, human and financial resources, and stakeholder engagements (*164,165*). These elements are not always available, particularly in low- and middle-income countries. For this reason, operationalization of value-based pricing often faces various practical challenges. Indeed, the capacity for authorities to undertake value assessment through health technology assessment and appraisal is highly variable in comprehensiveness and robustness (*108*). There are also differences in tools, procedures and methodologies, as well as duplication of efforts by government authorities and industry, prompting the European Commission to consider a proposal for better cooperation in relation to health technology assessment in the European Union Member States (*166*). Furthermore, many health technology assessments have been conducted, particularly in low- and middle-income countries, without the explicit purpose of informing the pricing of medicines (*108*).

Implementing health technology assessment to determine value and price of medicine requires strong technical capability, system capacity and a supportive politico-legal environment

3.3.1.3 Reference pricing

Reference pricing refers to the approach of understanding the appropriateness of prices of medicines based on selected benchmark prices, either from other jurisdictions (e.g. countries or other administrative regions) or a group of comparable medicines in the same system/formulary. The former is known as external reference pricing (ERP) or international reference pricing, and the latter is known as internal reference pricing (IRP) (*159*).

Unlike cost-based pricing and value-based pricing, reference pricing generally has lower data and resource requirements and its principles may be considered as relatively simple (*167*). It involves surveying the prices of a medicine to determine an appropriate benchmark price for that medicine. However, in practice, survey of medicine prices also requires technical expertise in design, data collection, analysis and interpretation. The purpose of reference pricing is to determine price or to inform further price negotiations. Key factors affecting the effectiveness of reference pricing include the following (*161,167,168*).

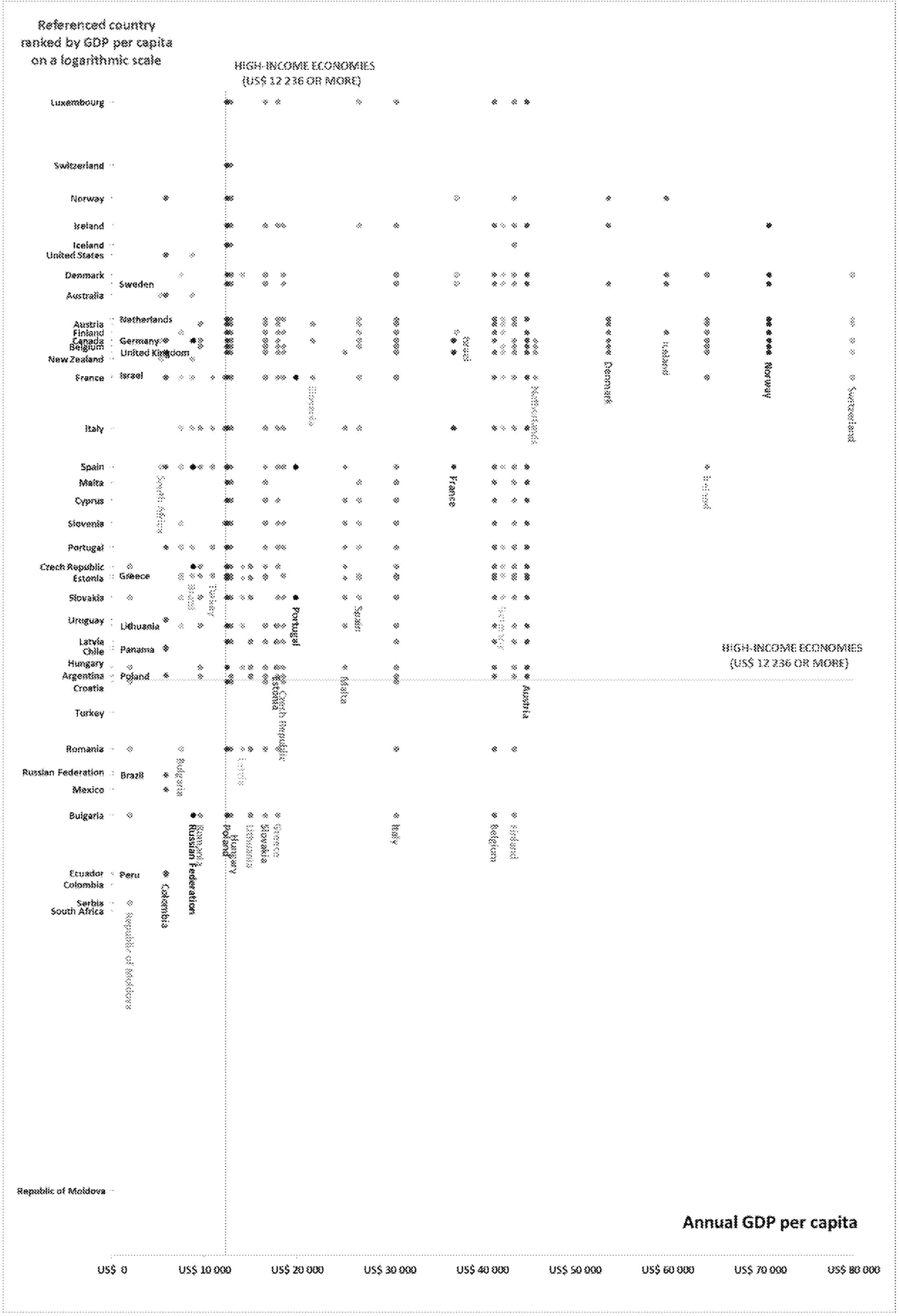
- Selection of appropriate benchmarks is perhaps the most critical part of reference pricing. Criteria for selection may include:
  - IRP: therapeutic comparability and interchangeability;
  - ERP: geographical proximity, country income (e.g. GDP), availability of medicines, country of origin.
- A range of calculation methods exist for determining an appropriate price from the selected set of reference prices. These include:
  - lowest price: Brazil, Bulgaria, Egypt, Hungary, Poland, Portugal (inpatient), Romania, Saudi Arabia, Spain, Thailand, Turkey, United Arab Emirates, Russian Federation, South Africa;
  - average price: Austria, Belgium, Jordan, Republic of Korea, Italy, Portugal (outpatient);
  - average of the lowest three prices: Greece, Czech Republic, Slovakia;
  - weighted price: Germany (based on market size and purchasing power parity)
  - other methods: France ("Prices similar to reference countries and not lower than the lowest price")
- Other methodological considerations include the type of price (e.g. ex-manufacturer price, consumer price), data source, exchange rates, frequency of price revision.

ERP has been widely applied in countries in Europe (*161,168*), and to a more limited extent in the Middle East (*169,170*), Latin America (*171,172*), Africa, and Asia (*171*). Differences in method and purpose have resulted in vastly different size and range of reference countries. As shown in Fig. 3.9 (p.37), countries with higher gross domestic product (GDP) per capita often seek price references from countries with comparable national incomes (e.g. Denmark, Iceland, Ireland, Norway, the Netherlands, Switzerland). In contrast, many countries with lower GDP per capita appear to have relied on price information from countries with a wide range of national incomes. As to be discussed in Chapter 4.2, this may reflect different timing of product launch in countries, and the considerable variability of prices, which has resulted in the need for a large sample of reference prices to better inform pricing decisions. Furthermore, differences in list price and (undisclosed) net transaction prices of medicine have diminished the effectiveness of ERP. The impact of such price opacity is discussed in Section 4.5.

> *Lower-income countries appear to have relied on prices information from countries with a wide range of national incomes, reflecting different timing of product launch and large price variability*

IRP has been used for regulating the prices of medicines with expired patent and after their market-exclusivity period ends (*173*). IRP has also been used to set the same price for selective medicines with the same or similar therapeutic effects, but without multiple brands due to a lack of competition or when the medicines still holds exclusive rights. For example, the New Zealand Government uses IRP for the pricing of oral contraceptives (*174*). In Australia, the prices of dasatinib and nilotinib were benchmarked to the price of imatinib 400 mg using a pre-determined therapeutically equivalent dose for the first-line treatment of chronic myeloid leukaemia (*175*).

Fig. 3.9: External reference pricing, by country and country GDP-per-capita ranking



Source: Author's visualization based on information from published literature (*167,171*)

3.3.1.4 Pricing based on tendering and negotiation

Tendering and negotiation are pricing approaches for determining the price that is mutually agreeable for both the sellers and the buyers. Tendering is a competitive bidding process whereby the winning tenderer would be awarded a contract for supplying a medicine or a set of medicines according to the agreed terms and conditions. The tendering process could be opened to all interested suppliers (i.e. open tender), or limited to a set of prequalified suppliers (i.e. restrictive tender) (*176*).

By its nature, tendering requires participation from at least two potential suppliers for medicines that are equivalent (e.g. generic and biologically similar medicines) or medicines with similar clinical therapeutic effects (i.e. so-called me-too medicines). Economic theory suggests that tendering may lead to lower prices insofar as the demand side has high purchasing power, and that accurate and detailed information on the relative attributes of pharmaceutical products and services on offer is available. In addition to price, other criteria for evaluating tenders include performance (e.g. financial capacity, ability to supply, past performance) and quality of products and services (e.g. certifications and timeliness) (*176*).

Negotiation can be used in combination with other pricing approaches (e.g. reference pricing and value-based pricing), with a view to reaching a final arrangement that would, ideally, present benefits to all parties involved. In contrast to tendering, negotiation is usually used when there are only few suppliers (i.e. monopoly or oligopoly for medicines under patent or a low number of registered products). Similar to tendering, high purchasing power and informational symmetry would ensure the usefulness of using this approach to establish a mutually acceptable price. Table 3.2 presents some of the examples where authorities have used tendering and negotiation for establishing the price of cancer medicines.

Table 3.2: Examples of tendering and negotiation for cancer medicines

Jurisdiction	**Medicine type**	**Description**
Ethiopia, Kenya, Nigeria, Rwanda, Uganda and the United Republic of Tanzania	Docetaxel, doxorubicin, epirubicin, fluorouracil, gemcitabine, leucovorin, methotrexate, paclitaxel; anastrozole, bleomycin, capecitabine, cytarabine, and vinblastine	The American Cancer Society and the Clinton Health Access Initiative negotiated with Pfizer and Cipla for the supply of 16 common cancer medicines in six large sub-Saharan countries (*177*). Under the agreement, Cipla expected to charge at or near production cost price while Pfizer planned to supply the products at prices sufficient to cover the cost of business, "as it seeks a sustainable model of philanthropy" (*177*)
China	Trastuzumab, bevacizumab, nimotuzumab, rituximab, erlotinib, sorafenib, lapatinib, apatinib, bortezomib, recombinant endostatin	In 2017, the Chinese Government reached agreements with pharmaceutical companies on the prices of 36 cancer medicines on the medical insurance list. These included 11 cancer medicines (*178*). Prices of all medicines were reduced by an average of 44% and up to 70% (*179,180*)
Italy	HPV vaccines for the prevention of cervical cancer	Since 2001, regional health authorities in Italy run tendering processes to encourage potential competition between the manufacturers for the bivalent and the quadrivalent HPV vaccines. This approach resulted in reductions in the ex-factory prices of these vaccines in 2007 to € 32.75–34.47, compared to € 95–104 negotiated by the Italian Medicines Agency (AIFA) (*181*)

Jurisdiction	Medicine type	Description
New Zealand	All medicines, including cancer medicines	The New Zealand Pharmaceutical Management Agency uses a combination of methods for purchasing medicines and determining medicine prices. These methods include negotiation and tendering (*174*)

Source: (*174,177,178,181*)

3.3.1.5 Price setting and profit control along the value chain

To control medicine prices, authorities in some countries have implemented regulations on mark-ups along the supply and distribution chains. The regulations may apply mark-ups to a base price (e.g. ex-manufacturer price), based on one or a combination of the following broad structures:

- regressive: decreasing amount or percentage of mark-ups with increasing base price;
- progressive: increasing amount or percentage of mark-ups with increasing base price;
- linear: same percentage mark-up for all prices;
- fixed: same amount of mark-up for all prices.

Table 3.3 shows examples of different mark-up structures and dispensing fees in selected countries.

Table 3.3: Mark-ups and dispensing fees in 2018, by jurisdiction

Jurisdiction (currency)	Mark-up structure in national currency			Dispensing fee
	Type	Base price and threshold	Mark-up level	
Australia (Australian dollar)	Regressive	Approved pharmacist price: • $ 0.00 to $ 180.00 • $ 180.00 to $ 2,089.71 • >$ 2,089.71	• $ 3.94 • $ 3.94 + 3.5% × amount >$ 180 • $ 72.43	$ 7.15
Denmark (Danish kroner)	Linear	All ex-wholesaler prices	• 35.5% (i.e. 1.25 × 1.084) + DKr 8.075 (1.25 × 6.46)	• DKr 10
Kenya	Linear	• All ex-manufacturer prices	• 8%	• Nil (public/ faith-based sectors)
New Zealand (New Zealand dollar)	Progressive[a]	Subsidy amount: • <$ 150 • ≥$ 150	• 4% • 5%	Information unavailable
South Africa (South African rand)	Regressive (with progressive dispensing fee)	Exit price: • R 0.00 to R 107.15 • R 107.15 to R 285.80 • R 285.80 to R 1000.33 • R >1000.33	• 46% • 33% • 15% • 5%	Maximum: • R 11.25 • R 24.00 • R 73.50 • R 172.00

Jurisdiction (currency)	Mark-up structure in national currency			Dispensing fee
	Type	Base price and threshold	Mark-up level	
Turkey (Turkish lira)	Regressive	Wholesale price:		Nil
		• TL 0 to TL 100.00	• 25%	
		• TL 100.01 to TL 200.00	• 16%	
		• TL >200.00	• 12%	

Note: [a] To cover the procurement and stockholding costs (for higher-cost medicines)

Source: Countries' department/ministry of health and (*182*)

Profit control is an effective measure to manage medicine prices insofar as the regulators have control over the supply of medicines at certain points along the supply chain. Typically, this means that the regulator needs to have full visibility of the supply and distribution chains. The regulator also needs to have the capacity and ability to enforce non-compliance. Profit control is most effective when there is a publicly-funded universal programme for the provision of medicines. In contrast, it may be much less effective in health care settings where the private sector plays a significant role in the delivery of medicines, or where the structure of supply chain is complex or under-developed (*183*).

Some countries may place limits on the frequency and magnitude of price increments, or even impose a price freeze or price reduction (*161,184*). In the latter, pharmaceutical prices cannot be raised for a predetermined period of time unless there is a justification. For example, since August 2010 (and at least until 2022), Germany has implemented a moratorium to halt price increase for medicines that are not subject to reference pricing, except for inflation (*185*).

In Canada, the Patented Medicine Prices Review Board requires holders of medicine patents "to file information about the prices and sales of their patented drug products in Canada at introduction and then twice a year until the patent expires", as set out by the Patent Act. The Board considers the average price of specific strength and dosage of a medicine to assess if a product is priced excessively according to the following criteria (*186*):

- the prices at which the medicine has been sold in the relevant market;
- the prices at which other medicines in the same therapeutic class have been sold in the relevant market;
- the prices at which the medicine and other medicines in the same therapeutic class have been sold in countries other than Canada;
- changes in the consumer price index;
- any other factors that may be set out in regulations.

The originator company may file a Voluntary Compliance Undertaking to express its commitment to adjusting the price of the patented medicine in question to a non-excessive level and offsetting any excess revenues, in compliance to the Board's guidelines. Medicines that have filed a Voluntary Compliance Undertaking include: panitumumab, pegaspargase, crizotinib, fulvestrant, busulfan, nilotinib (*187*).

Other countries have implemented price freezes as a measure to stabilize volatile medicine prices due to macroeconomic situations (e.g. Argentina (*188*)) or to contain costs (e.g. Pakistan (*189*)).

3.3.1.6 Other pricing measures relating to price setting

In addition to the approaches mentioned above for setting prices, pricing authorities may implement a range of measures to control prices and expenditure, which may directly or indirectly affect the eventual transaction prices of medicines.

For example, pricing authorities may set a maximum ceiling price to bind market prices to this upper threshold, rather than setting a fixed price for a particular medicine. In India, the National Pharmaceutical Pricing Authority sets ceiling prices for medicines listed on the National List of Essential Medicines by taking a non-weighted average of prices of different brands of the same medicine with more than 1% market share. For medicine with a single brand, the National Pharmaceutical Pricing Authority sets a price cap based on a fixed percentage calculated according to the prices of medicines in similar therapeutic categories (*190*). In the Netherlands, the Ministry of Health, Welfare and Sport sets maximum allowable prices for medicines determined through price references from Belgium, France, Germany and the United Kingdom (*191*). The market is free to set medicine prices below this threshold price.

Another method for setting medicine prices indirectly is the use of a Managed Entry Agreement (MEA), which has been commonly used for newer cancer medicines (*192*,*193*). MEA has been defined as:

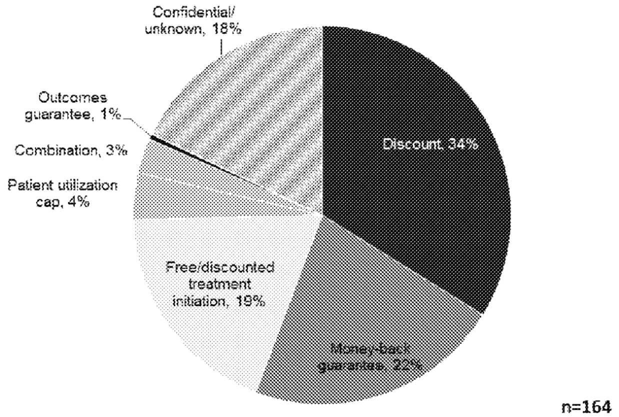
> an arrangement between a manufacturer and payer/provider that enables access to (coverage/reimbursement of) a health technology subject to specified conditions. These arrangements can use a variety of mechanisms to address uncertainty about the performance of technologies (e.g. clinical efficacy, efficacy and cost-effectiveness), and to manage the adoption of technologies in order to maximize their effective use, or limit their budget impact (p.79) (*194*).

A MEA has also been referred to as a risk-share arrangement to reflect its intent for sharing the risks – financial risks or uncertainties relating to performance – between payers and manufacturers. There are two broad types of MEA.

- Financial-based MEAs typically specify conditions directly relating to price (i.e. price discount and cap), volume or both. For example, in addition to using value-based pricing, authorities in Italy have implemented price-volume agreements to manage the price of “expensive, innovative drugs that involve large patient populations” (p.600) (*195*). The agreements set out a price–volume relationship agreeable to both parties (e.g. half the prices of evolocumab and alirocumab at every increase of 25 000 treated patients) (*195*). Financial-based agreements are commonly applied in other European countries for cancer medicines (*193*). MEAs generally impose confidential terms, but generally entail discounts, rebates, free stock and capping of utilization to a threshold volume or number of patients.
- Performance-based MEAs require payments to be contingent upon achieving certain pre-agreed health outcomes or other milestones when implemented. For example, a MEA may specify non-payment or discounts for patients who failed to respond to the treatment. It typically involves data collection through setting up registries or Phase IV trials (*196*). For example, the United Kingdom's National Institute for Health and Care Excellence (NICE) entered into an agreement with the manufacturer of bortezomib that the manufacturer was required to provide retrospective reimbursement to the payers for the costs of using bortezomib in patients who were subsequently identified as non-responders. In return, the manufacturer would receive payments at the normal price for further doses of bortezomib used in patients who have found to be responding to that medicine (*196*).

Fig. 3.10 shows the distribution of different types of MEA applied for cancer medicines in European countries. Discount, rebates and reduced price for treatment initiation were the most commonly used arrangements. Note that the specific arrangements of about two in five MEAs assessed in the study were confidential and unknown to the study authors (*193*).

Fig. 3.10: Types of MEA applied for cancer medicines in European countries



Source: (*193*)

MEAs can be in place for varying durations. For example, MEA are typically effective for two years (e.g. Italy, Belgium) to five years (e.g. the area of Scotland in the United Kingdom) unless there is a price decrease, or the manufacturer seeks extension.

The application of MEAs, particularly for performance-based MEAs, requires good governance to ensure the implementation is robust. Specifically, any conditions would need to be operationally manageable without having to dedicate a disproportionate amount of resources for complex monitoring and contract managements. For example, data collected as part of performance-based MEAs in the Netherlands were found to "poorly address the uncertainties that were left at the moment that reimbursement was filed in the Netherlands" (p.5) because of factors such as low quality of data and changing clinical practice (*193*). Indeed, the implementation of MEAs requires strong background support from information infrastructure, including the use of electronic health records to monitor patient health outcomes for the enforcement of performance-based MEA. Other challenges of MEAs (*197*) include:

Implementing Managed Entry Agreement could be complex, and the design would need to be operationally manageable.

- achieving distribution of risks acceptable to both the manufacturers and regulators (e.g. certainty of future payoffs);
- linking research measurement in specific clinical contexts to pricing arrangement;
- minimizing potentially high transaction and administrative costs;
- discouraging manufacturers from seeking higher prices in anticipation of a MEA; and
- Implementing appropriate arrangements that are clinically and politically acceptable to patients/clinicians, upon rescinding of a MEA due to failure to achieving a pre-agreed milestone.

A further measure that may reduce medicine price is tax reduction or exemption. Medicines may be subject to different taxes in countries that consider medicines like other consumer goods for the purpose of taxation. These include the application of import tariffs and value-added tax (VAT) (Table 3.4, p.43). Countries that are signatories to the reciprocal Pharmaceutical Tariff Elimination Agreement, or the "zero-for-zero" initiative, have 0% tariff (*198*). The zero-for-zero initiative has extended to some non-signatory countries, including low- and middle-income countries. Some countries have also implemented tax exemption specifically targeting cancer medicines. For example, from May 2018, the Government of China has exempted import tariffs on common medicines, including 16 cancer medicines (*199*). Such initiatives would require concurrent enforcement efforts to ensure that any savings from tax reduction or exemption are directly transferred to service providers or patients.

Many countries continue to apply tariffs on imported medicines, however, which may impair trade flow and access to medicines (*198*). Many countries also apply VAT to medicines, although VAT rates are generally reduced for medicines compared to the standard tax rates (*200*). Nonetheless, VAT can make medicines unaffordable while not substantially contributing to revenue goals (e.g. ≈1% of public revenue) (*198,201*).

Taxes can make medicines unaffordable while not substantially contributing to revenue goals

Table 3.4: Weighted average import tariffs and value-added tax for pharmaceuticals

Jurisdiction	Tariffs[a]	Value-added tax	Jurisdiction	Tariffs[a]	Value-added tax
Australia	0%	0%	**Mexico**	1.84–10%	0%
Brazil	7.06–11.43%	17%	**Nigeria**	0%	5%
Canada	0%	0%	**Norway**	0%	25%
China	3.75–6%[b]	16%	**South Africa**	0%	14%
Countries in European Union	0%	Variable (0–15% based on national laws)	**Russian Federation**	0% (Insulin) –5% (other)	10%
India	10%	5%	**Switzerland**	0%	2.5%
Indonesia	0% (Insulin) – 5% (other)	10%	**Turkey**	0%	8%
Japan	0%	8%	**USA**	0%	Variable (0–7%)

Note: [a] Weighted average for pharmaceutical products in categories HS300410, HS300420, HS300431, HS300439, HS300440, HS300450, HS300490; [b] Cancer medicines are exempted

Source: (198,200-202)

3.3.2 Monitoring, evaluating and adjusting prices

In countries with pricing regulations, authorities may monitor and revise medicine prices according to changing market conditions and therapeutic landscape. The most commonly employed method is revision of medicine prices upon the loss of market exclusivity of a product (Table 3.5). For example, through an agreement with the pharmaceutical industry, the Australian Government has set rules for reducing the prices of single-brand medicines listed on the Pharmaceutical Benefits Scheme (PBS) at 5%, 10% and 5% after 5 years 10 years and 15 years of listing, respectively (*203*). This presumably would ensure companies not accruing excessive returns for medicines with long periods of exclusivity. It might also incentivize the companies to work with clinicians for faster adoption of the medicines in clinical practice so as to maintain its profitability through increased volume.

Routine monitoring and revision of medicine prices ensure prices reflect market conditions

Table 3.5: Revision of medicine prices, by jurisdiction

Jurisdiction	Timing	Price reduction level
Australia	Number of years from first listing (without loss of exclusivity):	
	• 5 years	• 5%
	• 10 years	• 10%
	• 15 years	• 5%
	Loss of exclusivity:	
	• Entry of second brand	• 25%
	• Post-entry of second brand	• Weighted price from all competing brands
	One-off price reduction:	
	• 2006–2007	• Administrative price reduction of 12.5%
Belgium	Loss of exclusivity:	
	• Entry of first generic product	• 43.64% or 51.52% depending on reimbursement category
	One-off price reduction	
	• April 2012	• 1.95% reduction for all products or on products of the manufacturers' choice with equivalent saving
	• March 2015	• 6% price reduction for medicines in the reference-price group existing for ≥6 years
France	Loss of exclusivity	
	Non-biologic products:	
	• Entry of first generic	• 20% (original product)
	• 18 months after first generic	• 12.5% (original); 7% (generic)
	Biologic products:	
	• Entry of first biosimilar product	• 20% (original product)
	• 18–24 months after biosimilar	• 15% (Market share: 60–100%)
		• 10% (Market share: 40–60%)
		• 5% (Market share: 0–40%)
Norway	Loss of exclusivity	
	• Upon LoE	• 35%
	• 6 months after LoE	• 59–81%
	• 18 months after LoE	• 69–90%

Note: LoE=loss of exclusivity

Source: Countries' department/ministry of health and (*204*)

Price revision may also be considered when a medicine has extension of indications. In this case, some manufacturers and government authorities have used or proposed to use multi-indication pricing. This pricing approach aims to set distinct prices for the same medicine to reflect the differences in efficacy of that medicine when used for different conditions or in specific patient populations (*205–207*). Depending on the pricing arrangements, multi-indication pricing may either link the prices or discounts individually for each indication, or present a single price weighted for the anticipated utilization for each indication. For example, the manufacturer of everolimus marketed two brands with different prices in Sweden, for its use in preventing transplant rejection (SEK80 per mg) and oncology indications (SEK180 per mg) (*208*). In Switzerland, the rebate specified in a cost-sharing agreement for bevacizumab was only applicable when the medicine is used for lung cancer in low dose regimen (7.5 mg per kg) but not for other indications (*206*). In Italy, risk-sharing agreements for bevacizumab were applied on the basis of indication according to information collected through mandatory indication-specific registries maintained by the Italian Medicines Agency (AIFA) (*206*).

Some issues noted on this pricing approach include: (1) the importance of data availability and the costs associated with data collection to inform pricing; (2) the system's capacity to monitor utilization and administer or reconcile different prices by indication; and (3) that indication-based pricing, like price discrimination, may divert incentives towards higher-value indications, even though lower-value indications are important in absolute terms (*205–207*). Furthermore, it presents challenge for procurement because market prices of medicines are not differentiated by indication.

3.3.3 Measures to promote greater expenditure efficiency

3.3.3.1 Efficient dispensing and expenditure control

Some countries have also implemented pricing measures to seek greater efficiency in the use of cancer medicines. For example, the Australian Government has implemented a funding arrangement where the dollar amount of remuneration for chemotherapy administered through infusion or injection is calculated based on prices of the most cost-efficient combination of vial sizes that make up the patient's dose requirement (*209*). An example provided by the Australian Government authority is reproduced below (*210*):

> An authorised prescriber prescribes 150mg of a medicine that is available in vial sizes of 80mg and 200mg. The pharmacy dispensing software will use the algorithm to determine the most cost-effective combination of vials. If the most cost-effective option is 2 × 80mg vials, then the pharmacist would be paid for 2 × 80mg vials. If you are unable to dispense this combination, you are still able to use the 200mg vial to prepare the item. However, you would only be paid for the cost of 2 × 80mg vials.

Another pricing-related measure is implementing policies for cancer medicines with generic or biosimilar products, with a view to encouraging price competition. Table 3.6 summarizes the policies relating to prescribing and dispensing of generic or biosimilar medicines in various countries. Overall, policies relating to generic medicines are less restrictive than the policies for biosimilar products.

Table 3.6: Generic and biosimilar substitution policies

	Substitution		Prescribing using International Nonproprietary Names		Authorizing personnel: doctor or pharmacist	
Jurisdiction	**Generic**	**Biosimilar**	**Generic**	**Biosimilar**	**Generic**	**Biosimilar**
Australia	✓	✓	✓	✗	Pharmacist[a]	Pharmacist[a]
Austria	✗	✗	✗	✗	Doctor	Doctor
Belgium	✓ (M)	✗	✗	✗	Either	Doctor
Denmark	✓		✓	✗	Either	Doctor
Lebanon	✓	✗	✗	✗	Pharmacist[a]	Doctor
Finland	✓ (M)	✗	✓	✗	Pharmacist[a]	Doctor
France[b,c]	✓	✓	✓ (M)	✗	Pharmacist[a]	Pharmacist[a]
Germany[e]	✓	✓	✓	✗	Either	Either
Greece	✓ (M)	✗	✓ (M)	✗	Either	Doctor
Japan[d]	✓	✗	✗	✗	Pharmacist[a]	Doctor
Ireland	✓	✗	✓	✗	Pharmacist	Doctor
Italy	✓ (M)	✗	✓ (M)	✗	Either	Doctor
Netherlands	✓ (M)	✗	✓ (M)	✗	Either	Doctor
Poland	✓	✓	✓	✓	Either	Doctor
Portugal	✓ (M)	✗	✓ (M)	✗	Pharmacist	Doctor
Spain	✓ (M)	✗	✓ (M)	✗	Either	Doctor
Sweden	✓ (M)	✗	✓	✗	Either	Doctor
United Kingdom	✓	✗	✓	✗	Either	Doctor

Note: (M) = Mandatory; [a] Doctor and patients may prevent substitution. [b] Doctors are incentivized through a pay-for-performance scheme that includes generic substitution rate as an indicator, while pharmacists are incentivized through higher profit margins. [c] As of 2017, substitution of biosimilar was not implemented in practice even though it was introduced by law in 2014. [d] Financial incentives for pharmacists. [e] Biosimilar substitution is permitted for products from the same manufacturer

Source: (*161,211–215*)

Governments and insurers have also implemented non-price policies to ensure efficiency. For example, some countries require treating clinicians to obtain approval prior to prescribing or dispensing a select set of medicines, a practice known as prior authorization (*216–218*). Medicines may be selected based on criteria such as evidence-based guidelines, contractual agreements and costs. An important consideration for implementing prior authorization is to strike a balance between the level of administrative tasks to support such policies and timely patient access to treatment. For example, a process review in a breast oncology practice in the USA found that prior authorization was "complicated and labour intensive", and had limited impact on utilization because only 2.5% of prescriptions

Non-price policies could promote efficiency were non-compliant to standard of care (*216*). Thus, the successful implementation of prior authorization requires it to be fit-for-purpose and consensus-oriented (e.g. (*219*)).

Regular review of the list of medicines included for funding purpose is also an important step to ensure efficiency. For example, following two reviews of the clinical effectiveness and costs of medicines listed on the Cancer Drugs Fund List, National Health Service in England has removed 36 medicine-indication pairs of low therapeutic and economic values (*220*). Authorities in France also delisted medicines with overall low therapeutic value in 2002–2011, including a medicine for pancreas cancer that only extended survival by an average of 12 days (*221*). Main considerations for delisting medicines include the financial impacts on patients who have derived high therapeutic value from the removed medicine at an individual level; and changes in utilization of medicines remaining on the benefit list that are in a substitute therapeutic class to the removed medicines.

3.3.3.2 Pooled procurement

Pooled procurement refers to the arrangement where financial and non-financial resources are combined across various purchasing authorities to create a single entity for purchasing health products (e.g. medicines) on behalf of the individual purchasing authorities. The rationale for implementing such arrangement is twofold. Firstly, the arrangement generates purchased quantity higher than it would be otherwise possible for the individual purchasing authorities to achieve, thereby creating greater purchasing power through economies of scale and better position for negotiating lower prices for the procured goods. Secondly, the combined procurement process could potentially create greater efficiency through sharing of human resources (i.e. expertise and workload) and possible streamlining of procurement processes.

> *Pooled procurement aims to create greater purchasing power and streamline processes*

Pooled procurement has been used at subnational, national and international levels in various jurisdictions. For example, since 2008, the Government of Thailand has introduced pooled procurement for all medicines supplied under the "high-cost medicines E2 access program", which includes cancer medicines such as docetaxel, letrozole, leuprorelin acetate and imatinib (*222*). Under the procurement arrangement, the Government Pharmaceutical Organization manages centralized procurement and supplies medicines directly to hospitals upon request. Furthermore, hospitals can purchase medicines directly from pharmaceutical companies at centrally negotiated prices (*222*). Evidence shows that treatment costs per patient and annual health expenditures decreased substantially after policy implementation, mainly due to decreases in E2 medicines prices possibly from implementing pooled procurement and special purchasing arrangements with pharmaceutical companies (*222*). Evidence also shows an increase in the number of patients receiving specialty medicines (*222*). Further examples of pooled procurement at the national level are the voluntary centralized procurement systems implemented in Denmark and Norway for medicines used in hospitals (*223*). In Denmark for example, a public sector organization – Amgros – was set up to centralize tendering procedures and purchasing for all hospitals in the country. In parallel, the Danish Council for the Use of Expensive Hospital Medicines was established to assess the clinical costs and benefits of expensive medicines, with a view to guiding the selection of medicines by Amgros and clinicians. These centralized selection and procurement processes have resulted in sizeable financial savings (about € 314 million in 2015) for the Danish health care system (*224*).

At the international level, the Pan American Health Organization (PAHO) Strategic Fund was set up in September 2000 and is "contributing to the availability, quality and affordability of strategic public health supplies in the Americas" (*225*). The Strategic Fund provides pooled procurement of health products, quality assurance through a prequalification programme and collaboration with national medicine regulatory bodies, as well as financial support when required for ensuring continuity of supply. As of July 2018, 33 countries have signed agreements with PAHO to participate in the Strategic Fund (*225*). The Strategic Fund noted its achievement in lowering medicine prices through its procurement arrangement, including for cancer medicines. These include prices of between 3% and 1 395% lower than standard prices for cytarabine, docetaxel, doxorubicin, etoposide, ifosfamide and vinblastine (*225*).

There are a plethora of examples where such arrangement has been implemented at different scales (*226*). Nevertheless, the success of pooled procurement requires several facilitating factors particularly when the arrangement involves multiple jurisdictions. These include (*227*) the following.

- Political commitment is shared across the participating jurisdictions.
- Local needs of participating authorities (e.g. type of medicines, supply arrangements) should be reflected in the procurement arrangement.
- Legal, regulatory and policy requirements and processes would need to be aligned or have a common understanding (e.g. registration of products, quality assurance, patent laws, local production for subregional consumption).
- Sharing of information and experiences would help with capacity building and mitigating any risks and problems.

KEY POINTS

- **A suite of approaches for setting medicine prices along the value chain**: Payers have adopted a range of pricing approaches, individually or in combination, to set medicine prices. These include cost-based pricing, value-based pricing, reference pricing, and through tendering and negotiation, and regulating mark-up levels, as summarized in Table 3.7 (p.49).
- **Monitoring, evaluating and adjusting medicine prices throughout product life-cycle**: Some government authorities have routinely monitored medicine prices, with a view to adjusting prices throughout the product life-cycle. These include reassessing prices when there is a change in market conditions (e.g. entry of generic and biosimilar products) or therapeutic landscape (e.g. extension of indications for the same medicine). Government authorities have also undertaken other price and non-price-related approaches for achieving greater system efficiencies and for improving access.
- **Each to the system's own context**: The merits and disadvantages of individual pricing approaches must be interpreted with consideration to the countries' population needs and system requirements. Key considerations include technical aspects: choice of one or a combination of pricing approaches, data sources; and practical aspects: technical capacity, administrative capacity, timeliness and good governance.

Table 3.7: Summary of pricing approaches for medicines

Approach	Description	Method of price determination	Consideration
Setting medicine price			
Cost-based pricing	Setting price of a medicine based on the costs of inputs and add to it a mark-up percentage or amount	Assessment of costs through data collection and financial accounting. This may include the following elements: 1. Assessing relevant costs along a predefined scope along the value chain to the point at which the price would be set. The data may include direct material costs, direct labour costs, overhead costs associated with R&D, manufacturing, regulatory processes and compliance, communication, storage and distribution, dispensing and administration 2. Assessing and negotiating an acceptable level and structure of profit margin in addition to the costs	• Practicality of obtaining reliable data • Incentive to innovate and undertake production efficiently
Value-based pricing	Setting price of a medicine based on the differentiated worth/value of this medicine for a group of patients compared to the value of comparable medicines	Comparative assessment of value through health technology assessment or appraisals. These may include all or some of the following elements: 1. Assessing comparative health gains 2. Assessing comparative cost-effectiveness 3. Assessing affordability/financial impacts to the patient and health system 4. Assessing other (less quantifiable) factors, such as: severity of the medical condition; public health importance; confidence in the clinical evidence and assessment; equity of access; quality use of medicines; and societal value 5. Setting a price that is commensurate with the determination of "value"	• Scope of value dimensions • Measurement and enumeration of value, and their uncertainty
External reference pricing	Set price according to the prices in other comparable referenced countries/organizations	1. Select a set of comparable countries in which the medicine has already been launched 2. Obtain prices from these countries 3. Determine the price based on criteria such as average price, lowest price, and additional criteria (e.g. average of the four lowest prices)	• Choice of comparable reference countries • Calculation methods • Transparency of prices from reference countries
Internal reference pricing	Set price according to the prices of internal benchmark prices	1. Determine internal benchmarks: for example, budget constraint, prices of comparable medicines 2. Set or negotiate price	• Choice of medicines with the same or similar therapeutic effects

Approach	Description	Method of price determination	Consideration
Tendering and negotiation	Set prices based on the best offer received from tenderers	1. Identify and specify requirements for the supply of medicines, including: volume; timing and frequency of supply; quality assurance; and cap expenditure 2. Request for tender from the market (open tender) or preselected/qualified suppliers (closed tender) 3. Select the winning tender, and price by extension	- Number of potential suppliers - Selection criteria, including level of competition in the future
Profit control	Set and enforce levels of mark-ups in the supply and distribution chain	1. Determine the points along the supply chain at which price control can be enforced: wholesalers, pharmacies, dispensing doctors, and dispensaries 2. Determine/negotiate the structure and magnitude of mark-ups (e.g. fixed or regressive percentage) 3. Enforce and monitor mark-ups	- Visibility and level of control over the supply chain - Balancing the complexity of mark-up structure against ease of administration
	Set limits on the level and frequency of price increase	1. Determine/negotiate levels of price and frequency of price increase acceptable to the health system 2. Set threshold levels 3. Enforce and monitor price increase	- Negotiation power - Flexibility to accommodate price increase to ensure continuity of supply
Other approaches	- Setting ceiling price (only) - Using Managed Entry Agreement (MEA)	For MEA 1. Negotiate and specify conditions directly relating to finance (price ± volume) or performance (clinical outputs or pre-agreed health outcomes) 2. Implement MEAs according to agreed terms and conditions	- Balance of risks - Administrative requirements, including processes for negotiation and implementation - Transparency of prices and processes
Monitoring, evaluating and adjusting medicine prices throughout the product life-cycle			
Price revision based on changing market condition or therapeutic landscape	Revise prices upon entry of me-too medicines, or generic/biosimilar products	1. Determine/negotiate rules of price revision 2. If required, collecting price and utilization data 3. Revise prices according to data and rules	- Timeliness of price revision

Approach	Description	Method of price determination	Consideration
Other measures to ensure efficiencies	Efficient dispensing	1. Determine the most cost-efficient combination of vial sizes for injectable medicines to minimize wastage	• Calculation algorithm in the dispensing software
	Enhanced competition	1. Determine pricing, prescribing and dispensing rules for generic and biosimilar products	• Collection of data • Acceptance of policies by clinicians and patients
	Prior authorization	1. Selection of medicines for which authorization is required prior to dispensing	• Clarity of objectives • Ease of administration
	Regular review of benefit list	1. Selection of medicines for review according to certain criteria (e.g. therapeutic value) 2. Retain, amend or delist medicines according to review findings	• Capacity for undertaking reviews • Financial impacts to existing patients upon changes to listing criteria • Changes in utilization of medicines remaining on the benefit list due to substitution effect
	Tax reduction or exemption	1. Assess the appropriateness of the level of tariffs and taxes related to the supply of medicines 2. Apply tax reduction or exemption and ensure savings are transferred to consumers	• Impacts on tax revenues and medicine prices
	Pooled procurement	1. Seek alignment in the goals for arranging pooled procurement 2. Combine financial and non-financial resources across various purchasing authorities to create a single entity for purchasing health products 3. Seek to lower prices of medicines and stability of supply through economies of scale and stronger negotiating power 4. Monitor the progress of the arrangement against the goals and make modification accordingly	• Shared political commitment • Reflecting local needs (e.g. demand and supply arrangements) • Harmonization of legal, regulatory and policy requirements and processes • Sharing information and experiences among participating authorities

3.4 Summary

This chapter presents a range of approaches applied for the pricing of cancer medicines. The main points are summarized below.

i. **Pricing policy for cancer medicines may encompass the following objectives:**

- Equitable and timely access: patients in need should have access to cancer medicines in a fair and timely manner without compromising the quality and safety of medicines.
- Affordable access: patients should be able to afford cancer medicines over the full course of treatment.
- Health system sustainability: spending on cancer medicines should not divert resources away from the provision of other essential health products and services.
- Good governance: pricing and procurement process should observe the principles of transparency, efficiency and accountability.
- Balanced incentives: policies should align its intended objectives with the goals of different stakeholders, which may include appropriate prescribing and dispensing, R&D and industry development.

ii. **Industry's pricing of cancer medicines is largely driven by commercial goals, with little or no observable relationship with inputs to the value chain, including R&D:**

- The market structure of cancer medicines is characterized by imperfect competition, with evidence of individual companies holding monopoly over specific cancer therapeutic areas. This has resulted in pricing and supply strategies explainable by the economic theory of monopoly.
- Marginal costs of production of medicines are relatively small compared to their prices.
- Case studies indicate that pharmaceutical companies set prices not with the aim to realize the full value potentials of cancer medicines through improved access.
- With an average return of US$ 14.50 in revenue per dollar invested for R&D, cancer medicines, through high prices, have generated returns for the originator companies far in excess of the R&D costs and other factors of production.

iii. **Pricing authorities have adopted a range of pricing approaches to set and manage prices of medicines throughout value chain:**

- Pricing authorities have set medicine prices based on the costs, value, external and internal price references, and through tender and negotiation. This may be accompanied by the application of MEAs to manage expenditure and uncertainties of clinical value.
- Pricing authorities have monitored medicine prices, with a view to controlling prices throughout the supply chain and product life-cycle.
- To encourage system efficiency and affordability of medicines, pricing authorities have also implemented measures such as pre-authorization, efficient dispensing and tax exemption.

In view of the discussion presented above, the following chapter discusses the possible impacts of pricing approaches, or the lack thereof.

4 Impacts of pricing approaches or lack thereof

This chapter first discusses the possible impacts of pricing policies on the price, availability and affordability of cancer medicines. It presents evidence from countries with different income levels and extents of price regulation. Where appropriate, comparative analyses are presented to show the relative impacts.

The chapter then examines whether high financial returns on investment might have had a positive or negative impact on the R&D of cancer medicines. It also examines how confidential rebates and discounts could affect market transparency, leading to other problems that might compromise good governance. Finally, it discusses whether high financial returns from cancer medicines and other incentives might have resulted in consequences that would deviate from the original policy intent, or even contravene the law. These include expansion of indications in cancer medicines initially approved with an orphan drug designation; incidence of medicine shortages; emergence of substandard and falsified cancer medicines; and the appearance of inefficient, unethical or illegal business practices.

This chapter should be read with the following clarifications in mind. Firstly, this chapter does not aim to provide a definitive answer about whether an observed outcome could be solely attributed to a particular pricing policy. This is because causality is multifactorial; a range of complex system components could affect medicine prices and other policy outcomes, intended or otherwise. Furthermore, some observations on medicine prices and outcomes are pertinent only to a point in time or for a specific context. For this reason, some evidence presented may not be generalizable to all contexts and across time. While this chapter offers explanations and interprets the potential implications from the evidence presented, readers should consider their respective system contexts and experiences, and interpret the evidence accordingly.

4.1 Impacts on price

4.1.1 Price level

It is well documented that prices of many cancer medicines are high in absolute terms. The annual costs of cancer medicines introduced in the past decades are often at least in the tens of thousands of US dollars per patient (*28,33,50,228,229*). As noted previously, high prices and high costs of cancer medicines have motivated a fervent debate about the appropriateness of pricing policies globally (Sections 1.1.2 and 1.1.3).

In relative terms, comparative evidence shows that prices and costs of cancer medicines are higher than the prices and costs of medicines used in other therapeutic areas. For example, a pricing study of biological medicines approved by the US FDA from 1997 to 2016 found that the median annual cost of monoclonal antibodies was significantly higher when used in oncology and haematology (US$ 142 833), compared to the next highest priced therapeutic categories: immunology (US$ 53 969); infectious disease and allergy (US$ 29 808); ophthalmology (US$ 22 464); and cardiology and endocrinology (US$ 15 624) (*230*).

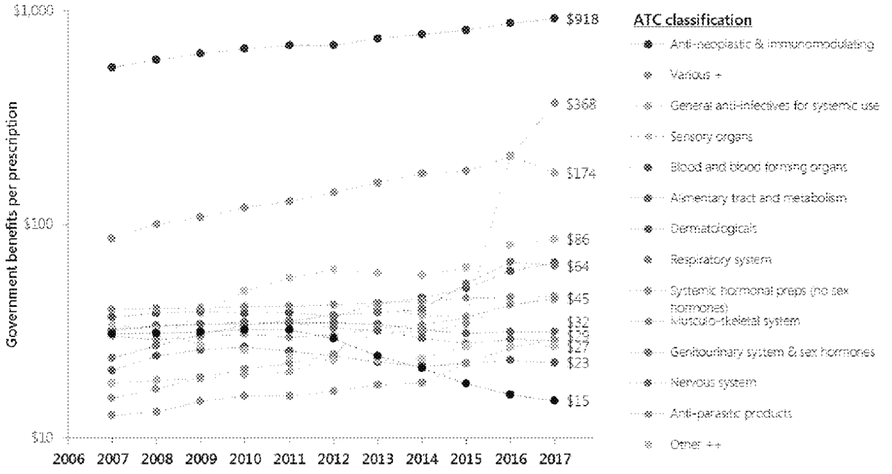
Prices of many cancer medicines are high in both absolute and relative terms

Administrative data from various insurance schemes confirm the higher spending on cancer medicines compared to other therapeutic areas. For example, the administrative data from the Australian Government

PBS show that the per-prescription cost of cancer medicines was at least 2.5 times higher than the average cost of medicines for other therapeutic areas over the past decade (Fig. 4.1a). An analysis of data from the Norwegian Prescription Database over the past 10 years also gives a similar observation, where the supply of anti-neoplastic and immune-modulating medicines was by far the highest source of revenue per patient for retail pharmacies in Norway (Fig. 4.1b).

Fig. 4.1: Comparative expenditure on cancer medicine in (a) Australia and (b) Norway

a. Pharmaceutical Benefits Scheme, Australia (in Australian dollars^{a})

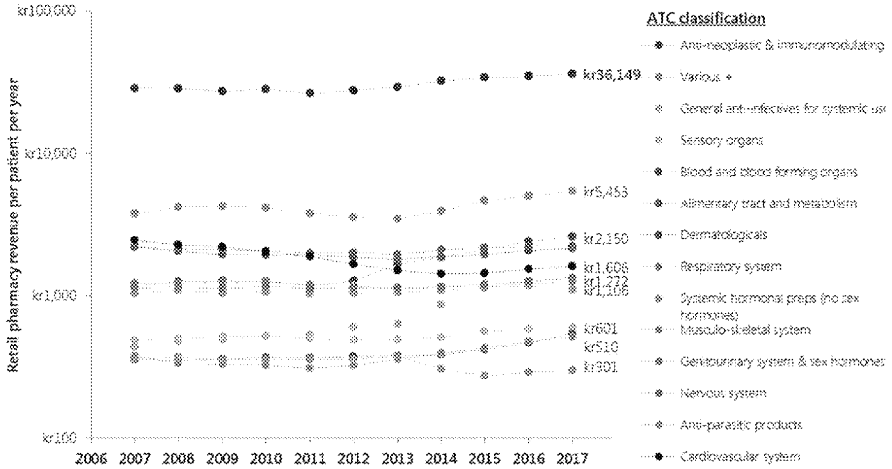


Note

Various+ includes allergens, diagnostic agents, urine test reagents, food supplements: lactose, amino acid preparations.

Other++ are extemporaneously prepared items and/or PBS items with no ATC equivalent

b. National Health Insurance Scheme, Norway (in Norwegian kroner^{a})



Note

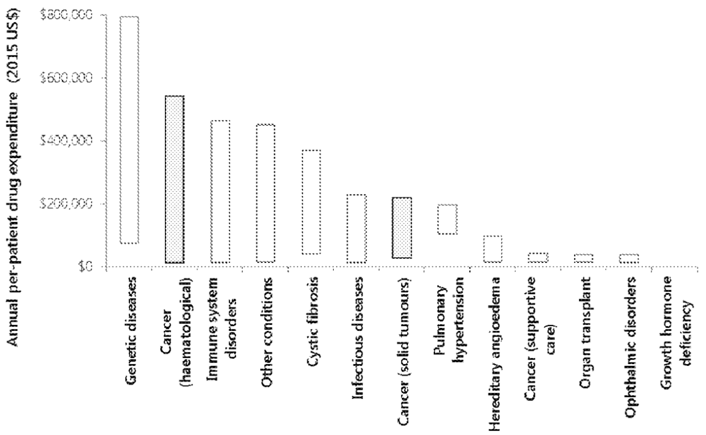
Various+ includes allergens, diagnostic agents, urine test reagents, food supplements

Note: ATC=Anatomical Therapeutic Chemical; ^{a} In 2017, one US dollar was equivalent to 1.305 Australian dollars and 8.272 Norwegian kroner (*231*)

Source: Medicare Statistics (*232*), the Norwegian Prescription Database (*233*)

In the USA, America's Health Insurance Plans examined 150 specialty drugs with annual expenditure of at least US$ 10 000, which included 63 cancer medicines. It found that these specialty drugs incurred 30% of the total expenditure on prescription medicines despite only accounting for 2% of all prescriptions (*234*). Among the specialty medicines included, the annual per-patient expenditure on cancer medicines was among the highest, with ranges between US$ 27 000 and US$ 220 000 for treatments of solid tumours, and between US$ 13 000 and US$ 541 000 for treatments of haematological cancers (Fig. 4.2).

Fig. 4.2: Comparative expenditure on high-cost specialty medicine in the USA



Note

Bar indicates the price range

Genetic disease includes hereditary hypercholesterolaemia

Immune system disorders include multiple sclerosis

Source: Adapted from America's Health Insurance Plans (*234*)

These observations bring to question whether the significantly higher spending on cancer medicines compared to other therapeutic areas is justifiable. This is pertinent, considering that society does not always consistently support a preference for health gains in cancer compared to other health conditions (*54*). Besides, some cancer medicines can only deliver marginal clinical benefits to individual patients, possibly less than the patients' expectation in absolute magnitude and relative to the costs of medicines (*235*).

4.1.2 Price variation

Some degree of price variation across markets is within expectation according to economic theories. Firstly, the "law of demand" indicates an inverse relationship between price and quantity for most goods, where the quantity demanded would fall according to the level of price increase and the market's sensitivity to changing price (i.e. price elasticity of demand). This means that prices may vary across settings depending on the quantity demanded. Similarly, the "law of supply" predicts a proportional relationship where the quantity supplied would rise according to the level of price increase and price elasticity of supply. Laws of supply and demand are broadly true at least for commodities in a simple market, but it would be rendered less relevant in explaining prices in more complex markets where a range of factors would lead to market failure. These include asymmetric information[ix] and non-competitive market structure, which are common phenomena in the medicine market. These additional factors would make medicine prices less predictable.

Secondly, the "law of one price" states that, after accounting for transaction costs and trade barriers, identical goods would be sold for the same price in trading countries when their prices were expressed in a common currency. Accordingly, the price of a medicine in different countries should in theory be the same when expressed in a common currency (e.g. US dollars) after adjustment for their respective purchasing powers. However, in nominal terms (i.e. prior to adjustment), prices of medicines directly observed in different markets should vary. Again, government regulations, market conditions and market failure could result in prices deviating from what would be expected in theory.

[ix] Asymmetric information occurs when one party (e.g. pharmaceutical companies and health care professionals) to a transaction has more or superior information compared to the other party (e.g. consumers).

In the context of cancer medicines, several studies have presented evidence showing that current pricing policies (or the lack thereof) have led to considerable variability in the prices of cancer medicines within a country and across regions (Table 4.1). These studies showed that the observed variability in cancer medicine prices did not seem commensurate with the demand, nor the country's purchasing power. For example, based on 949 procurement transactions between 2010 and 2014, a study found that the procurement prices of EML cancer medicines were generally higher in African countries compared to Latin American countries, despite having comparable levels of income (*236*) (Table 4.1 and Fig. 4.3). Even within a specific region, the prices of cancer medicines bear little relationships with the demand (using cancer incidence as a proxy) and the country's ability to pay (using the per-capita income level as a proxy). An example is the prices of EML cancer medicines in Rwanda and the United Republic of Tanzania (Fig. 4.3, p.57). The median price in Namibia also seems to be much higher than one would expect from its country income and demand (Fig. 4.3, p.57).

> *Studies showed that observed variability in cancer medicine prices did not seem commensurate with the demand, nor the country's purchasing power*

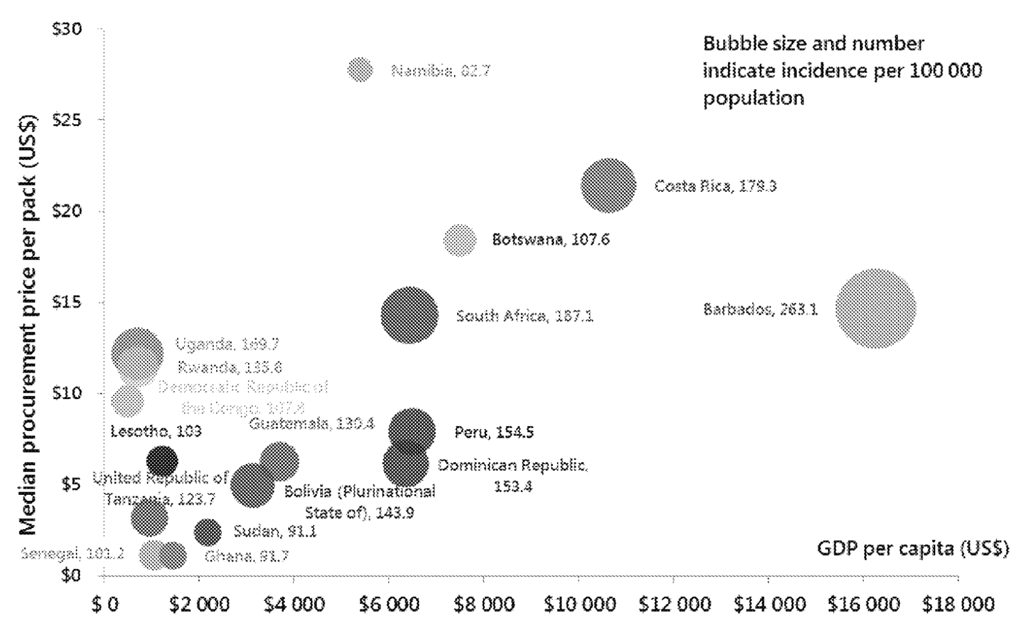
Table 4.1: Studies that examined price variability of cancer medicines

Author (year)	Scope	Key findings
Cuomo (2017) (*236*)	**Jurisdiction**: 29 countries from Africa, the Caribbean and Latin America **Setting**: 19 national and international buyers **Time frame**: 2010–2014 **Medicine**: Cancer medicines in the 19th Essential Medicines List	The procurement prices recorded in 949 transactions suggested that some countries and regions (e.g. in Africa) have paid more for essential cancer medication than others (e.g. Latin America)
Kolasani (2016) (*237*)	**Jurisdiction**: India **Setting**: End-consumer prices listed in Current Index of Medical Specialities **Time frame**: January–April 2016 **Medicine:** 23 multiple-brand anti-cancer drugs manufactured in India	There are wide percentage price variations of different brands of the same medicine: • oxaliplatin 50 mg ±125.0% • methotrexate 2.5 mg ±75.3% • paclitaxel 260 mg ±147.0% • flutamide 250 mg ±714.24% • imatinib 100 mg ±5.56% • granisetron 1 mg ±388.7%
Salmasi (2017) (*238*)	**Jurisdiction**: 10 countries from South-East Asian, Western-Pacific and East-Mediterranean regions **Setting**: Listed retail unit prices with adjustment for purchasing power **Time frame**: 2016 **Medicine**: 26 anti-cancer drugs of similar form, strength & pack size	The prices of anti-cancer drugs were highly variable in the regions studied, with the following distribution of high-to-low price ratios: • <3 14 drugs (53.8% of sample) • 3–6 8 drugs (30.8%) • >6 4 drugs (15.4%)

Author (year)	Scope	Key findings
Vogler (2016) (*239*)	**Jurisdiction**: 16 European countries, Australia, and New Zealand **Setting**: official list prices per unit at ex-factory price level **Time frame**: February–June 2013 **Medicine**: 31 cancer medicines; all but two medicines (gemcitabine and zoledronic acid) were originator medicines	The difference of a drug price between the highest priced country and the lowest priced country varied between 28% and 388%, with the following distribution: • 28–50% 10 drugs (32% sample) • 50–100% 16 drugs (52%) • 100–200% 3 drugs (10%) • >200% 2 drugs (6%)

Source: (*236–239*)

Fig. 4.3: Median prices of EML cancer medicines, by country income and cancer incidence



NOTE: Prices were recorded and analyzed from 2010 to 2014 but not standardised to a reference year.

Source: (*236*)

The implications of the significant dispersion of prices are at least threefold. Firstly, it indicates that existing procurement practices in some countries may not be the most efficient, as lower prices could have been achieved. Secondly, it may impair the countries' coverage of essential cancer medicines when prices are higher than their ability to fund and provide the medicines. This would, in turn, have a negative impact on patients' timely access to medicines and their ability to achieve the best possible health outcomes. Thirdly, regional price differences within a country may cause inequitable access, with only some patients having access to the medicines at lower prices.

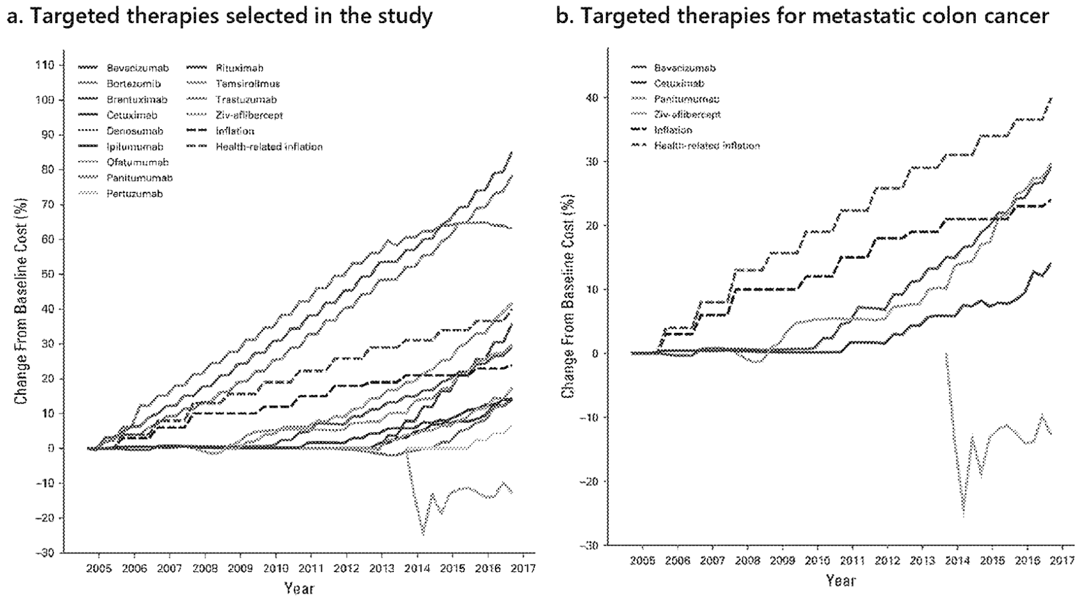
4.1.3 Could a lack of consistent price regulation lead to uncontrolled medicine prices?

Evidence suggests that a lack of effective and consistent policy for managing medicine prices across the value chain and over time could result in uncontrolled and highly dispersed prices for the same medicine.

A lack of uniform pricing policies may result in ineffective control of medicine prices and cost-shifting activities

For example, the largely market-based health care system in the USA has seen significant price escalation in cancer medicines in recent years, possibly due to a lack of price control policy. For example, a study of the prices of 24 patented, injectable cancer medicines approved by the US FDA between 1996 and 2012 found that, except for ziv-aflibercept[x], all other medicines had their prices increased significantly during the study period (Fig. 4.4a, p.58). The average cumulative change in the monthly treatment costs over an average of 8-year follow-up, after adjustment for general inflation, was +19.1% (95% CI: +11.0–27.2%) (*147*). The study also examined the pricing dynamics among four potentially-competing targeted therapies for metastatic colon cancer (Fig. 4.4b, p.58). Except for ziv-aflibercept, the monthly costs of cetuximab, panitumumab and bevacizumab increased despite the supposed competition among these medicines (*147*). A lack of price competition among comparable cancer medicines has also been observed in the prices of imatinib, dasatinib and nilotinib (*240,241*).

Fig. 4.4: Cumulative percentage change from baseline mean monthly cost in the USA, by year



a. Targeted therapies selected in the study

b. Targeted therapies for metastatic colon cancer

Source: (*147*) (Reproduced with permission)

These observations suggest that a market-based approach for managing medicine prices in the absence of appropriate government intervention may not bring about sufficient price competition (*242*). Instead, pharmaceutical companies often engage in non-price competition, for example, through advertising, sales promotion and preferential contractual arrangements, which may not be welfare-enhancing. It is worth noting that the uncontrolled and significant price escalation of cancer medicines in a large market like the USA could distort international price expectation.

Uncontrolled and significant price increases of cancer medicines in a large market like the USA could distort international price expectation

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[x] The price of ziv-aflibercept (Zaltrap) dropped significantly following an article in the New York Times that took a stance against its "phenomenally expensive" price (*29*),

A lack of uniform pricing policies within a health care system may also result in ineffective control on medicine prices. For example, a study in Mozambique found that Government's policy on specifying fixed statutory profit and cost ceilings for medicines in 2004–2005 had not been applied evenly across the supply chain because of a lack of oversight on policy implementation and collusion among wholesalers and pharmacies (*243*). This had led to mark-up levels from wholesalers and pharmacies contributing to a higher proportion of the final medicine price than the policy had initially intended (62–78% vs 56–58%) (*243*).

Finally, a lack of consistent pricing policy across service delivery settings within a health care system could result in cost-shifting activities and inequitable patient access. For example, a USA study examined insurer payments for infused cancer chemotherapy during 2004–2014 for patients with private health insurance. It found that the spending was much higher when chemotherapy was provided in a hospital outpatient department compared to physician office settings at all levels of analysis: line-item drug level (US$ 3799 vs US$ 1466), treatment-day level (US$ 7973 vs US$ 3502) and 6-month treatment-episode level (US$ 84 660 vs US$ 43 700) (*244*). In parallel, this study observed a significant shift in the provision of chemotherapy services towards hospital outpatient departments, with the proportion of chemotherapy being infused at hospital outpatient departments (6% to 43%) directly corresponding to a decline in the proportion provided at physician offices (about 90% to 55%) (*244*). This example demonstrates that inconsistent pricing policies in different settings of a health care system could create perverse incentives for potentially inefficient service delivery.

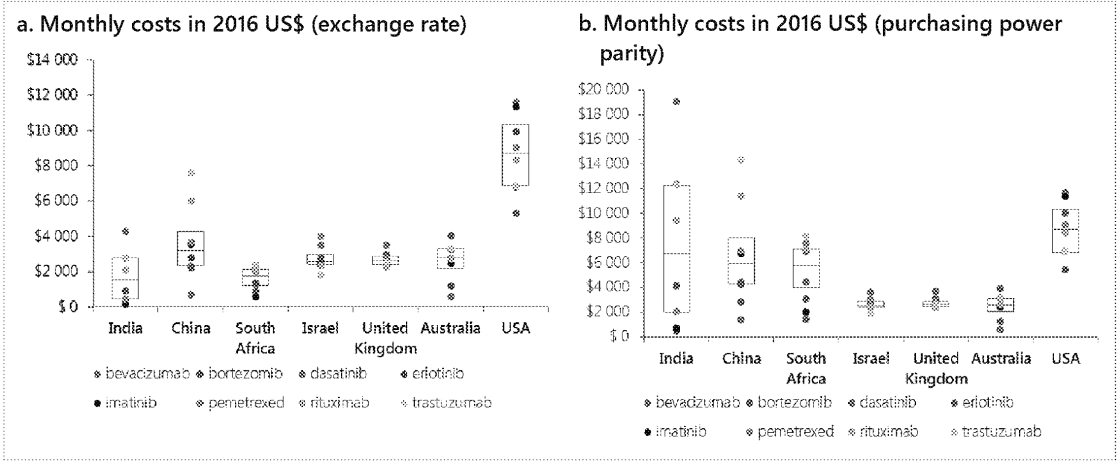
4.1.4 Could price regulation lead to lower prices?

Comparative studies on the prices of cancer medicines suggest that having a higher degree of pricing regulation may result in lower medicine prices and costs.

For example, a study compared the costs of eight patented cancer medicines – bevacizumab, bortezomib, dasatinib, erlotinib, imatinib, pemetrexed, rituximab, trastuzumab – in Australia, China, India, Israel, South Africa, the United Kingdom, and the USA (*245*). The monthly costs of these medicines, estimated based on prices expressed in US dollars using currency exchange rates, suggested that prices in the USA were typically higher than in other countries (Fig. 4.5a, p.60). When the prices were adjusted for the differences in national income levels and purchasing powers in buying goods and services, the analysis showed that monthly costs of these medicines in the USA, India, China and South Africa were, on average, higher and more dispersed, than in Israel, the United Kingdom and Australia (Fig. 4.5b). The lower and less variable prices in the latter three countries might be associated with the range of regulatory measures implemented to manage medicine prices. These measures have also been implemented more comprehensively in methodology and frequency than in the former four countries. These include pricing informed by health technology assessments as well as undertaking formal price negotiation and regular price revision.

> *A higher degree of pricing regulation may result in lower medicine prices and costs*

Fig. 4.5: Costs of cancer medicines (a) without and (b) with adjustment for purchasing power



Note: The boxplots show the median and interquartile prices across the selected targeted therapies

Source: (*245*)

To further illustrate the possible association between stronger price regulations and lower medicine prices, an analysis was undertaken to compare the real price indices for pharmaceuticals in Australia and the USA from 1981 to 2017. This index indicates the change in price level for pharmaceuticals relative to the change in price level for all goods and services (i.e. all-item consumer price index) against a nominated baseline year (i.e. 1981). These two countries were chosen for illustrative purpose because of their contrasting health care systems and approaches for managing medicine prices: the Australian Government is known to have implemented a range of pricing policies for medicines over the past decades for its single-payer national pharmaceutical insurance scheme – the PBS; the USA on the other hand is known for its market-based health care, with multiple private and public insurers and with minimal government intervention for the pricing of medicines.

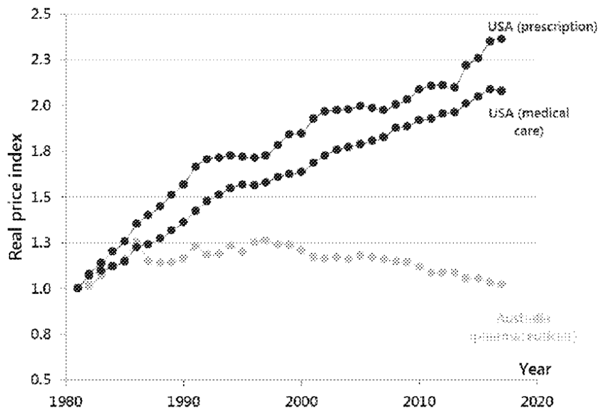
The comparative analysis shows that in the early 1980s, both countries had similar overall price trends where prices of pharmaceuticals grew faster than the collective prices of all goods and services (Fig. 4.6a, p.61). However, the trends in the two countries began to diverge in the late 1980s where the price level of medicines continued to rise faster in the USA, while the growth rate of pharmaceutical prices in Australia seemed to have been stabilized at around 10% higher than the consumer price index. This could possibly be due to the introduction of "cost effectiveness" as a requirement before listing a medicine on the national pharmaceutical insurance scheme, so as to ensure the benefits of a given medicine were high enough to justify the price requested by the manufacturer (*246*). The divergence became more prominent when the Australian Government undertook further reforms of its national scheme after 2005 (*247*), which was implemented in response to a report that warned "in 40 years' time, the PBS could account for 3.4% of GDP, making it the largest part of the Government's spending on health" (*248*). The reforms seem to have resulted in gradual normalization of the growth rate of medicine prices in Australia to a level in line with the overall inflation rate of other consumer goods (Fig. 4.6a). In contrast, medicine prices continued to grow considerably in the USA, with the cumulative growth reaching 2.4 times the overall inflation rate of other consumer goods in 2017. Of note, the price level of prescription medicines in the USA rose in parallel with

Pricing and reimbursement policies in Australia over four decades have controlled the growth rate of medicine prices.

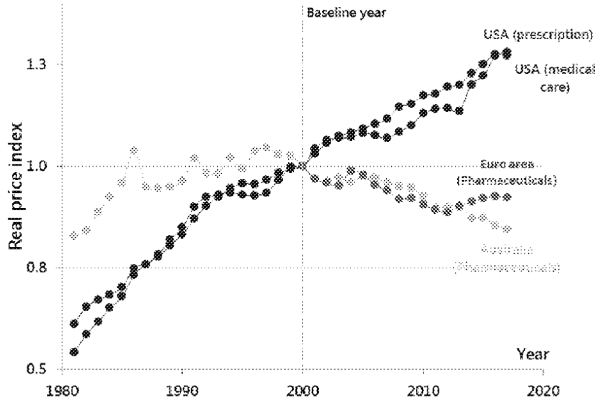
the price level of medical care (Fig. 4.6a). This suggests that the rising price trend in the USA was across all medical goods and services under the same conditions of market-based policy environment. Considering this, the rise of pharmaceutical prices in the USA is unlikely to be a result of pricing policies in other countries, as suggested in a recent policy paper (*48*).

Fig. 4.6: Cumulative real pharmaceutical price inflation in (a) Australia and US with year 1981 as the baseline year (b) Australia, US and Euro area with year 2000 as the baseline year

a. Baseline year=1981 (i.e. Index=1 in 1981)



b. Baseline year=2000 (i.e. Index=1 in 2000)



Note: The index was calculated by dividing the pharmaceutical price index by all-item consumer price index in the baseline year; the term "Euro area" comprises EA11-2000, EA12-2006, EA13-2007, EA15-2008, EA16-2010, EA17-2013, EA18-2014, EA19 (see footnote xi)

Source: Author's calculation based on data published by the Governments of Australia (*249*), the USA (*250*) and Eurostat (*251*)

A similar trend has also been observed from the price indices in Europe. Based on the harmonized indices on consumer prices and pharmaceutical prices available from 2000, Fig. 4.6b shows that pricing regulations on medicines in Euro-area countries[xi] had also kept medicine prices from rising faster than general consumer prices (i.e. Index <1.0) relative to the consumer price index in 2000. However, it is important to note that there are considerable differences in the structures of health care systems and pricing arrangements among the Euro-area countries. In fact, prices of medicines have grown faster than consumer goods in some European countries in recent years (e.g. Austria, Germany, not shown).

[xi] European Union Member States which adopted the Euro as their common currency, started with 11 countries in 2000 (EA11: Austria, Belgium, Finland, France, Germany, Ireland, Italy, Luxembourg, Netherlands, Portugal, Spain) to 19 countries in 2017: https://ec.europa.eu/eurostat/statistics-explained/index.php/Glossary:Euro_area_enlargements

The overall growing trend of pharmaceutical prices in the USA presented above is broadly in line with the price trend of cancer medicines reported in the literature. For example, a study has noted that the median monthly costs of cancer medicines at the time of US FDA approval had grown at about tenfold in real terms every 20 years between 1970 and 2010 (*229*).

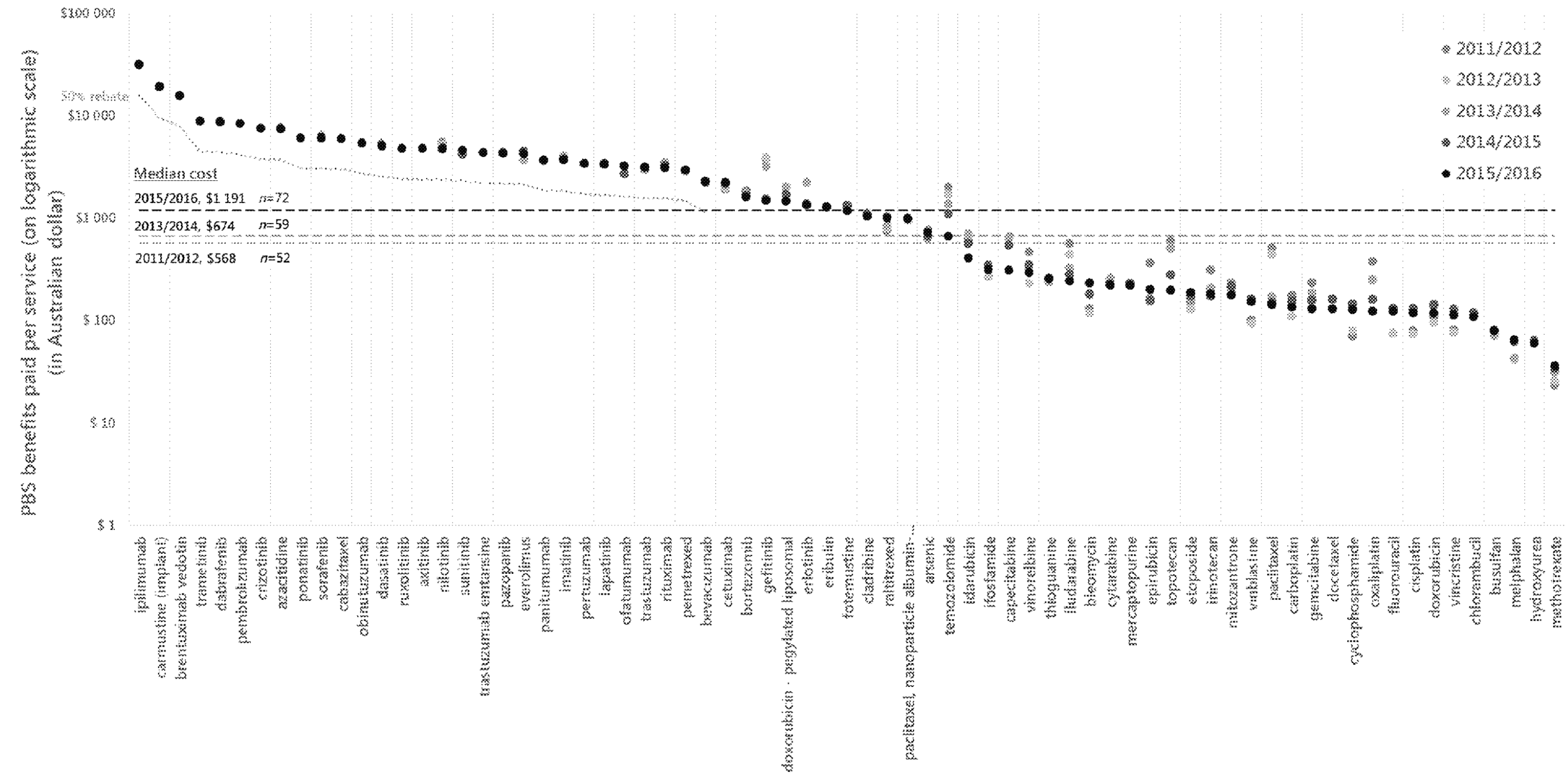
In contrast, while the overall growth of pharmaceutical prices in Australia has been normalized by price regulations to a level in line with that of other consumer goods, the unit costs of cancer medicines seem to have grown exponentially in recent years, similar to the global trend. To this point, Fig. 4.7 (p.63) shows the average benefits paid by the Australian Government for the supply (also termed a "service") of cancer medicines between 2011 and 2016, dispensed under Australia's national pharmaceutical insurance scheme (the PBS). Plotting on a logarithmic scale, the analysis shows that the per-service costs of newer cancer medicines were substantially higher than the per-service costs of older conventional chemotherapy (Fig. 4.7, p.63). Overall, the median per-service cost across all PBS-reimbursed cancer medicines has grown from 568 Australian dollars in 2011–2012 (about US$ 550) to $ 1191 in 2015–2016 (about US$ 1050). This represents a compound growth rate of 16% per year. This growth was most probably driven by the high prices of newer cancer medicines because:

- the PBS has implemented pricing policies to reduce the prices of (older) generic cancer medicines and has only rarely increased the prices of medicines (e.g. only upon application by the manufacturer with evidence of increased costs of manufacturing, or to ensure supply continuity for medicines in shortage). This is shown in the right side of Fig. 4.7 (p.63);
- accounting for rebates and discounts provided by pharmaceutical companies to the Australian Government for newer cancer medicines under risk-sharing agreements would reduce the per-service costs. However, as shown in the blue-dotted line in Fig. 4.7 (p.63), the per-service costs for these medicines remain significantly above the median costs, on a logarithmic scale;
- the magnitude of possible benefits conferred by the newer medicines (e.g. survival benefits, reduced side-effects and dosing frequency) are unlikely to be higher than standard of care (e.g. chemotherapy) on a logarithmic scale. As discussed in Chapter 2, some newer cancer medicines have only demonstrated marginal benefits and may in fact cause more harms to patients than an improved standard of care. A recent study also found that prices of cancer medicines in the USA have grown disproportionately to their clinical benefits (*252*).

In summary, even in countries that have implemented a range of policy measures to manage medicine prices, the prices of newer cancer medicines have grown substantially over the past decades, possibly disproportionate to their intrinsic and comparative values for patients and health care systems. This suggests that more measures may be needed to realign the prices of cancer medicines to their absolute and comparative values, with a view to expanding patient access to cancer medicines and ensuring the long-term financial sustainability of health care systems.

> *Prices of newer cancer medicines have grown substantially over the past decades, even in countries that have implemented a range of pricing measures*

Fig. 4.7: Australian Government's reimbursement for cancer medicines dispensed (2011–2016)



Note: The analysis was undertaken at the molecule level to account for all dosages and dose forms. In Australia, clinicians typically prescribe or dispense quantity sufficient for a month or a course of treatment, as specified in the Schedule of Pharmaceutical Benefits. In Australia, the Government financial year is from July to June of the following year

Source: Author's calculation based on Medicare Australia Statistics (253)

4.1.5 Price and market competition

As presented in Section 3.3.2, various countries have implemented policies to facilitate price competition among pharmaceutical companies for medicines that are clinically substitutable (i.e. me-too medicines, generic and biosimilar products). In general, price and market competition has led to lower prices of generic brands compared to their originator counterparts. In Europe, market entry of generic medicines would, on average, result in 20% lower price than the originator brand in the first year, and a further 25% in the second year (*254*). In the USA, the first generic medicine typically enters the market at a price 20% to 30% lower than the branded medicine, with cumulative price reduction of up to 80% over time (*254*). Price competition upon market entry of generic medicines has also been observed for cancer medicines. For example, in Latvia, the annual cost of generic imatinib (€ 1 238) was reportedly 96% lower than the cost of originator brand (€ 29 835) (*255*). In India, generic paclitaxel, docetaxel, gemcitabine, oxaliplatin and irinotecan were priced between 8.9% and 36% of their branded equivalents (*256*).

Policies to facilitate price competition for clinically-substitutable medicines have resulted in lower prices and expenditure savings

Lower prices of generic medicines have translated into expenditure savings. For example, a modelling study in the United Kingdom estimated that increasing generic prescribing saved the United Kingdom National Health Service £ 7.1 billion between 1976 and 2013 (*257*). This corresponded to 490 million more items to be dispensed without an increase in the total spending (*257*). Another study found that switching selected originator medicines to the lowest-priced generic equivalents would on average achieve expenditure savings of 9% to 89% (*258*). In Brazil, market entry of generic medicines saved approximately US$ 5 billion for the health care system between 2001 and 2007 [cited in (*254*)]. In India, generic paclitaxel, docetaxel, gemcitabine, oxaliplatin and irinotecan have generated an estimated savings of about ₹ 47 billion (US$ 843 million) in 2012 (*256*).

However, the extent to which pricing policies could enhance competition and reduce medicine prices is dependent on a range of market and policy factors. For example, while the Australian Government has implemented a range of policies to enhance price competition among off-patent medicines, various comparative studies have found prices of generic medicines in Australia to be higher than the prices in other countries (e.g. (*259,260*)). Another example is the pricing policies for generic medicines in Europe, which typically set maximum prices or reimbursement rates, with or without benchmarking to the prices of the corresponding originator brands through reference pricing (*261,262*). A narrative review found that reference pricing for generic medicines in Europe typically resulted in very rapid, if not immediate, reduction in prices. However, by the policy design, prices only fell to the highest regulated level, with typically small price reduction as more competing companies entered the market, unless there were frequent adjustments to the reference prices reimbursement rates (*218*).

Several market and policy factors influence the effects of pricing policies on competition and medicine prices

Indeed, a range of contextual factors may jointly influence the overall magnitude of price reduction upon introduction of pricing policies for generic medicines or on-patent me-too medicines. These include the following.

- Existing price or non-price policies
    - Price reduction would be greater in settings where there are policies to mandate generic substitution. Reduction would also be greater when there are frequent adjustments to the price benchmarks (e.g. maximum reimbursement rate and lowest price as the reference) (*263*).
    - The magnitude of price reduction following market entry of generic medicines may be lower in countries with stronger price regulations on branded medicines. This is because the lower prices of branded medicines prior to generic entry might diminish the marginal savings that could be gained through generic entrants (*264*). Policy-makers may consider the potential trade-off between earlier price reduction of branded medicine against larger price reduction from generic medicines later.
- Number of competing companies/products/indications and market size
    - A greater number of generic products would enter the market when the market potential is large (*218*,*265*). As the number of generic entrants rises, medicine price would fall, and the price of the originator brand would fall more than the prices of generic brands. A modelling study suggests that the overall prices of generic medicines would remain above the long-term marginal costs of production until there were at least eight competing companies in the market (*265*). This means that price competition may not be optimized unless there are many competing companies or products.
    - Expansion of indications for on-patent medicines may result in further consolidation of market dominance, while the approval of me-too medicines may increase price competition. For example, a study on the prices of orally administered cancer medicines approved by the US FDA in 2000–2012 found that prices of these medicines in the USA rose 5% annually in 2007–2013. The study observed that the prices increased an additional 10% with every supplemental US FDA-approved indication. In contrast, price was reduced by 2% with every additional US FDA approval of a competing me-too medicine (*151*).
    - Savings from the falling prices might not necessarily be transferred to the consumers or government authorities (*262*).
- Regulatory requirements and processes
    - As discussed in Section 3.2.2.2, despite efforts towards international harmonization of regulatory requirements for biosimilar products (*133*,*134*), varying rules regarding nomenclature and substitution in some jurisdictions may have created barriers for the introduction of these products, indirectly reducing the level of price and market competition.
    - High application costs and lengthy regulatory review of generic and biosimilar medicines had also been noted as limiting factors that may hinder the speed of market entries of generic and biosimilar products. For example, the lack of price competition for imatinib and filgrastim in the USA has been noted to be due partially to a lack of availability for generic and biosimilar products (*242*). In Japan, market penetration of generic cancer medicines in 2010–2016 was found to be competitive, but not for antimetabolites, protein kinase inhibitors, hormones and monoclonal antibodies (*266*).

Furthermore, pricing policies need to work in conjunction with the enforcement of robust competition policies and good governance in order to reap the full benefits of competition, as well as to prevent anti-competitive behaviours and other business practices that may impair system efficiency. Anti-competitive business practices have been observed in the cancer medicine market. These include the following examples.

- Introduction of pseudo-generics: A pseudo-generic medicine is an additional brand marketed (usually) by the originator companies for their own branded medicine, but priced lower than their branded medicine. This business practice may discourage other genuinely generic medicines from entering the market because of reduced market share. To put it simplistically, the development of pseudo-generic involves the following steps: "take a generic drug, repackage it and add marketing and hey presto you have a branded generic" (*267*). Originator companies have at least three advantages over potential generic entrants: (1) existing knowledge on the evidence, market, and production; (2) "first-mover advantage" because of the ability to market the pseudo-generic product before patent expiry or loss of market exclusivity; and (3) existing relationship with prescribers through the branded product. An example is the introduction of a generic version of azacitadine supplied by its originator (Celgene) but contracted by Celgene to Sandoz AG to sell (*268*). Moreover, it is worth noting that the originator and their contracting companies may refer to the marketed generic medicines as "branded generics" or "quality generics" to seek differentiation from other genuinely generic medicines, despite the latter having equally met the necessary regulatory requirements for quality. In addition to reduced competition, prices of pseudo-generics may not be as low as genuine generics, thereby diminishing the overall savings to the health care system.

- Tacit or actual collusion: Price competition is typically motivated by the competing firm's desire to increase market share and profits in the long term. There are economic explanations (e.g. through game theory) and examples in economic history to indicate that repeated price reductions against rivalling companies may create business uncertainties and produce worse commercial outcomes for the competing companies. Thus, to avoid competition and maintain stability, competing companies may engage in explicit or tacit agreement (i.e. collusion) either by fixing price at high level or sharing the market, at the expense of consumers and society. For example, in a legal case lodged in 2017, the Attorney Generals of 45 states and the District of Columbia in the USA have alleged that 18 generic companies and subsidiaries have engaged in price fixing and market sharing for 15 medicines, including zoledronic acid[xii] (*269*).

- "Product hopping": This involves "a brand-name company switching the market for a drug, prior to its patent expiration date, to a reformulated version that has a later-expiring patent, but which offers little or no therapeutic advantages" (*270*). For example, a study argues that the originator company of filgrastim has employed this strategy by developing pegfilgrastim – a single-dose version of daily filgrastim[xiii]. The originator promoted and transferred the sales to the single-dose version before the launch of competing biosimilar products to filgrastim (*271*).

- The "principal agent problem": In many countries, the provision of health care services requires strong governance to ensure clinicians, as the co-called agents for the patients and health care system, are acting in their best interest. This is because health care professionals who prescribe or dispense the medicine do not pay for the medicine, while patients or health systems pay for the medicine but do not choose it. In the absence of adequate monitoring and governance, any benefits arising from competition may not end up benefiting patients or health systems. For example, prior to 2007, the

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[xii] Indicated for patients with multiple myeloma and patients with documented bone metastases from solid tumour.

[xiii] The comparative benefits of filgrastim versus pegfilgrastim remain equivocal. While systematic review found better toxicity profile in favour of pegfilgrastim (*411*), two head-to-head double blind randomized controlled trials did not observe statistically significant differences in efficacy and safety between pegfilgrastim and filgrastim (*412,413*).

Australian Government had been paying more than the market price for generic medicines, because manufacturers sold medicines to pharmacists for less than the government list price. To correct the system deficiency, the Australian Government introduced a pricing arrangement called "price disclosure" that mandates the manufacturers to disclose their selling prices and volumes, so that the government could adjust and align the list price according to the market price (*272*). Similar observations regarding discounts not being transferred to the consumer price had also been noted in other countries (*262*).

- Wasteful non-value-added activities (i.e. rent-seeking activities): Companies may also engage in wasteful non-value-added activities such as lobbying or filing patent clusters to delay generic/biosimilar entry. Economic theory indicates that such rent-seeking practices are more likely when the rent-seeker aims to gain excessive returns or when existing returns are high (i.e. to prevent loss of existing high return). For example, the inception of the United Kingdom Cancer Drugs Fund in 2010 involved political lobbying from patient groups and the pharmaceutical industry (*273*). This initiative was intended to provide patients in England faster access to cancer medicines that were (1) available on the market but not yet appraised by NICE; (2) not recommended by NICE on the basis of cost-effectiveness after appraisal; and (3) used outside of marketing authorizations (i.e. so-called off-label use) (*274*). This programme essentially diminished the role of NICE in ensuring efficient use of public funding and allowed medicines of little clinical and economic benefits to bypass the funding requirements. Indeed, this programme was later found to have cost the United Kingdom Government £ 968 million between 2010 and 2015 (*45*); overspent the allocated budget for 2014–2015 by 48% (*45*); failed to deliver "meaningful value to patients and society" (*275*); and did not expedite access to new cost-effective cancer agents prior to NICE approval (*276*).

KEY POINTS

- **Prices of cancer medicines are high** not only in absolute terms, but also relative to prices of medicines used in other therapeutic areas.
- **Prices of cancer medicines are variable within countries and across regions**. The variation bears little relationship to the demand for these medicines, and the patient or health system's ability to pay.
- **Pricing measures applied by government are necessary.** There is evidence showing that (1) prices of cancer medicines grew significantly in the absence of regulations; (2) non-uniform pricing policies have led to differences in medicine prices, resulting in inefficient cost-shifting activities and potential inequity in access; and (3) greater level of price control can lower prices.
- **There are approaches for promoting competition among medicines that are substitutable clinically**. For example, me-too medicines, generic and biosimilar products have resulted in lower prices and expenditure savings. However, the magnitude of impact is variable because of contextual factors such as (1) existing pricing and non-price policies for branded medicines; (2) number of competing companies/products and market size; and (3) regulatory requirements and processes for generic and biosimilar medicines.
- **The effectiveness of pricing policies would be enhanced by having robust competition policies and good governance** to prevent anti-competitive and efficiency-impairing business practices, such as introducing pseudo-generics; engaging in tacit or actual collusion; product hopping; and wasteful non-value-added activities such as lobbying or creating patent clusters to delay generic/biosimilar entry.

4.2 Impacts on availability

Different health care settings have vastly different system capacity and the populations they serve have varying epidemiological profiles. For this reason, the availability of cancer medicines (or lack thereof) should be understood within the context of individual health care systems. Specifically, it is important to recognize that some cancer medicines may not be as necessary or even useful in certain contexts (e.g. in the absence of companion diagnostic tests for genetic profiling, or technical skills and labour for safe prescribing and administration). Furthermore, as mentioned, some cancer medicines may confer only marginal benefits and cause more harms to patients in the absence of appropriate supportive care. For this reason, the lack of availability of these cancer medicines would be less pertinent than cancer medicines listed on the EML which have been selected following robust assessment of their public health relevance, evidence on efficacy and safety, and to some extent, comparative cost-effectiveness. Finally, like many studies on the availability of medicines, the data often only represented the availability of medicines at one point in time (i.e. cross-sectional data) and might not indicate the persistence of (non-)availability. It is with these caveats in mind that this section presents existing evidence on the availability of cancer medicines.

> *The availability of cancer medicines (or lack thereof) should be understood within the context of individual health care systems*

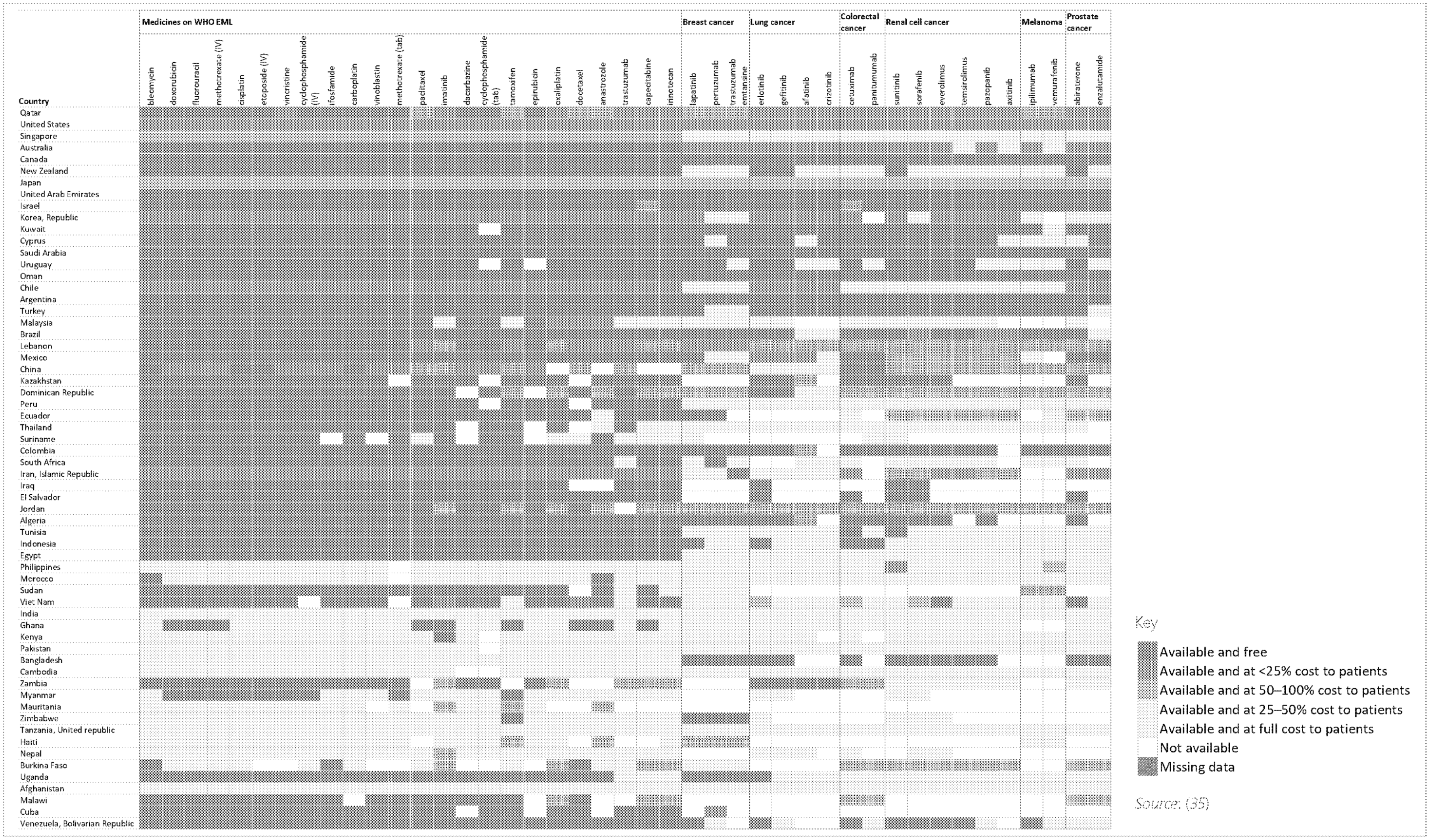
4.2.1 What is the overall availability of cancer medicines?

To date, the most comprehensive assessment on the availability of cancer medicines globally is presented in two studies that surveyed the availability of oncology medicines in the national formularies of 49 European countries in 2014 (*55*) and 63 countries outside of Europe in 2016 (*35*). The online surveys enquired about the availability of medicines on the national formularies (with or without pairing to an indication e.g. imatinib for gastrointestinal stromal tumour) and the extent to which the availability was subject to patient out-of-pocket payment.

Of the oncology medicines surveyed, the study data in both non-European (Fig. 4.8, p.69) and European countries (Fig. 4.9, p. 70) showed a trend that countries with lower income, as indicated by GDP per capita, had lower availability of medicines, or availability only with higher patient out-of-pocket payments. This trend is particularly prominent for higher-cost medicines, including medicines that require genetic profiling (e.g. trastuzumab and erlotinib). The study found that 32.0% and 57.7% of EML cancer medicines were available to patients in lower-middle-income and low-income countries, respectively, only if the patients were to incur the full costs (*35*). Two of the most commonly cited barriers for the national formularies to provide better access to these medicines were the lack of reliable suppliers and budget capitation (*35*). Observations from these surveys suggest that the prices of cancer medicines at which the suppliers were willing to supply was higher than the prices that health systems could afford.

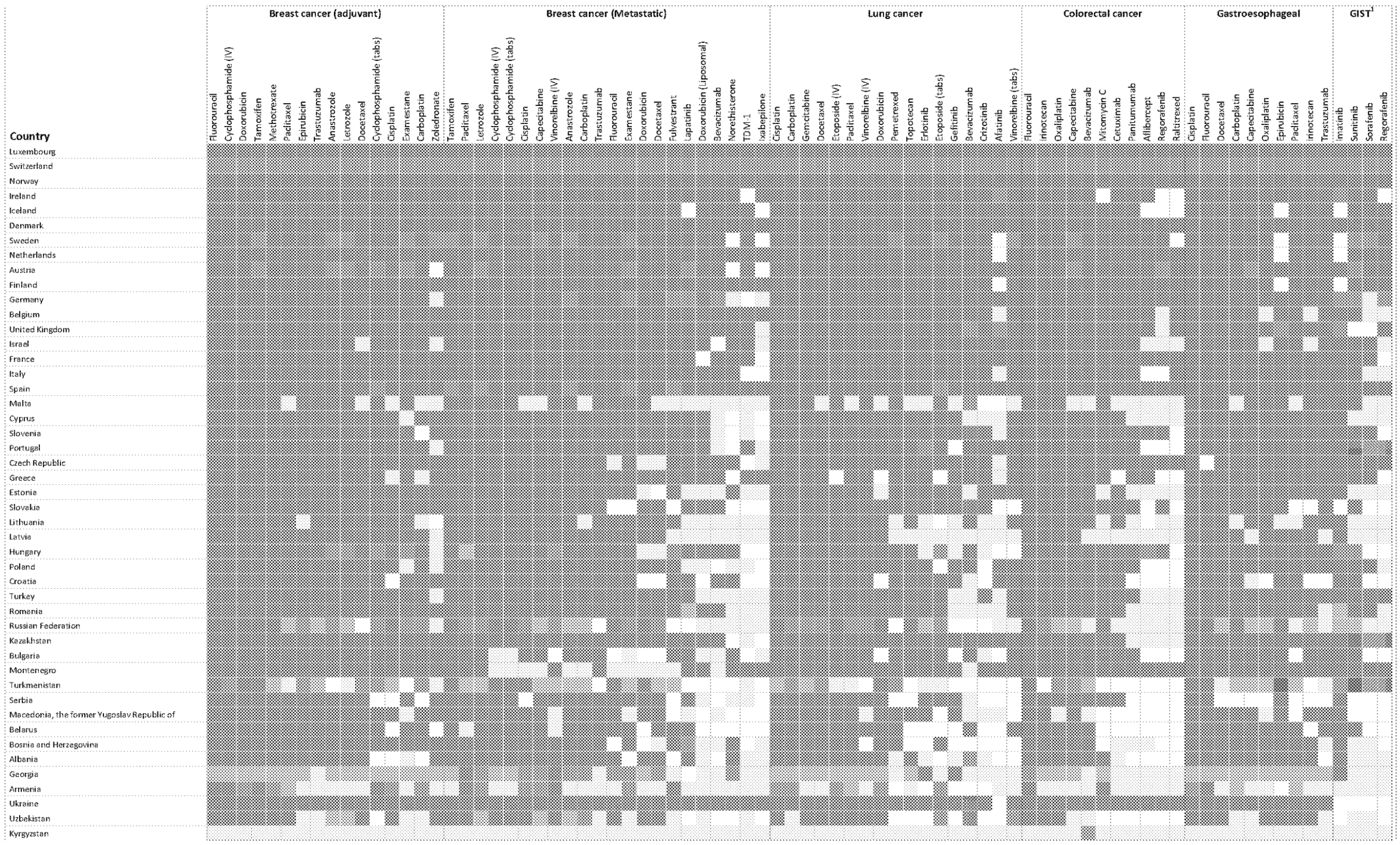
> *Countries with lower income had lower availability of cancer medicines, or availability only with higher patient out-of-pocket costs*

Fig. 4.8: Availability of cancer medicines in national formularies of non-European countries in 2016, by country ranked by GDP per capita in 2016



Source: (35)

Fig. 4.9: Availability of cancer medicines in national formularies of European countries in 2014, by country ranked by GDP per capita in 2016



Note

[1]Gastrointestinal stromal tumour

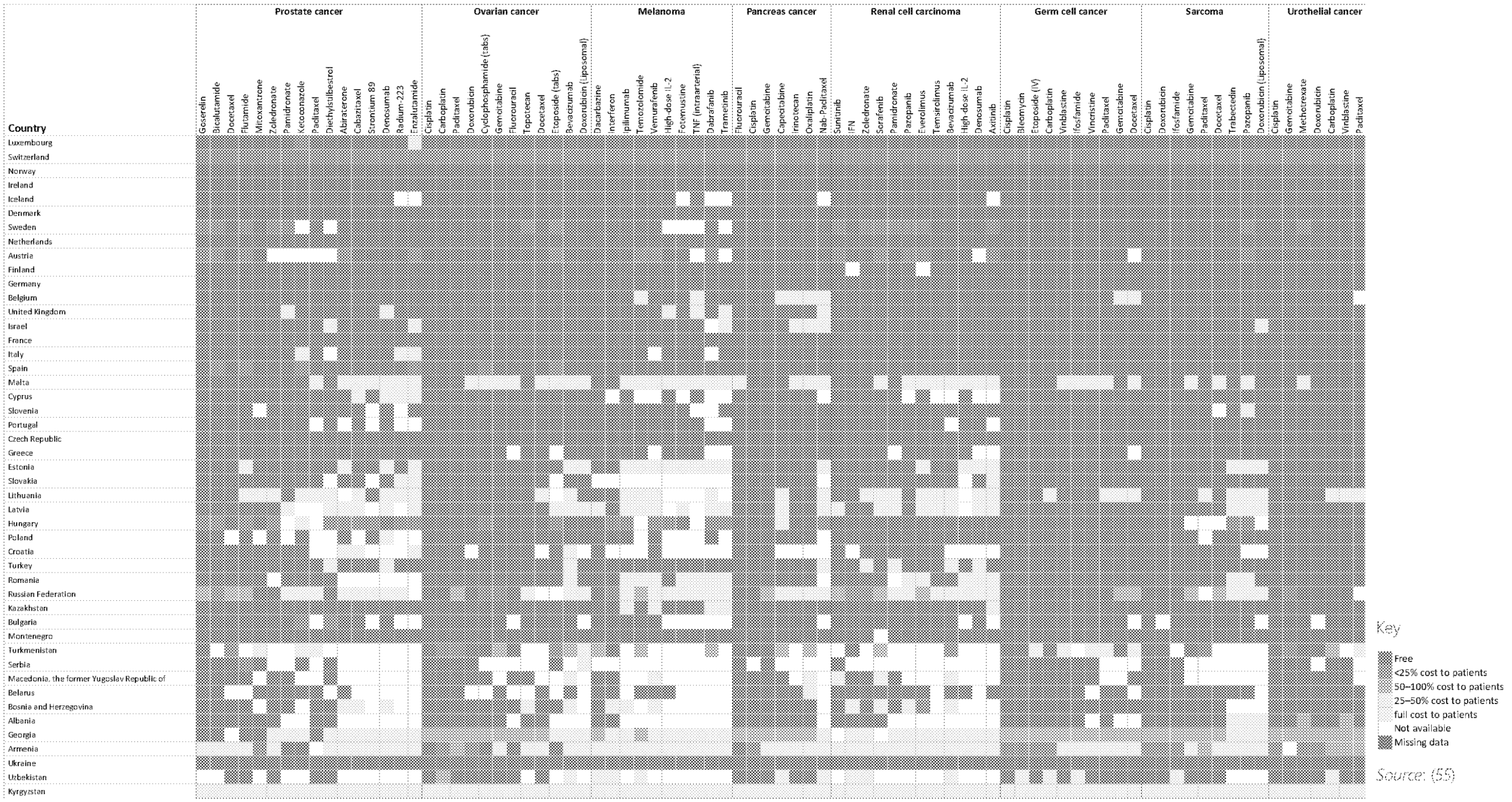
Key

▨ Free
▨ <25% cost to patients
▨ 50–100% cost to patients
▨ 25–50% cost to patients
▨ full cost to patients
▨ Not available
▨ Missing data

Source: (55)

[CONTINUE]

Fig. 4.9: Availability of cancer medicines in national formularies of European countries in 2014, by country ranked by GDP per capita in 2016



Source: (55)

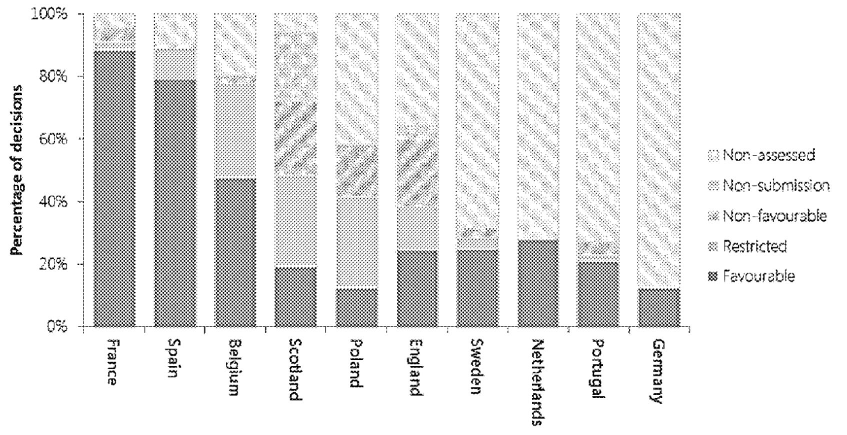
The low availability of cancer medicines has also been noted in other country-specific studies that included medicines for haematological cancer. For example, a 2017 survey in Pakistan (Punjab) found that the overall availability of 40 cancer medicines was relatively low: higher-priced originator brands were available in 52.5% of the surveyed facilities, while the lowest-price generics were available only in 28.1% of the facilities (*277*). The availability of these medicines was higher in private hospitals and pharmacies (71.9% for originator brands and 20.0% for lowest-price generics) than public hospitals (31.4% for originator brands and 11.7% lowest-price generics) (*277*). The disparity in availability suggests potential inequity in patient access to cancer medicines in this region.

Another study assessed the selection of cancer medicines in national essential medicines lists in 76 non-high-income countries in 2013 (*278*). It found that the national formularies surveyed had a median of 16 cancer medicines. Similar to the findings of other studies presented above, low-income countries typically had the least number of cancer medicines listed on the formulary (11 medicines) compared to lower-middle-income (18 medicines) and upper-middle-income (26 medicines) countries (*278*). However, this study observed considerable variation in availability even among countries belonging to the same income grouping. The study also observed significant variations in the number of cancer medicines listed on national formularies across WHO regions. It found that the Western Pacific and African Regions had the least number of medicines listed at medians of 3.5 and 12 medicines, compared to at least 17.5 medicines in non-high-income countries surveyed in other regions (*278*). The survey also found that 68% of the national essential medicines lists surveyed did not have any medicines in the "hormones and related agents" category. Newer cancer medicines, including targeted therapies were infrequently incorporated (*278*).

4.2.2 Have high costs of cancer medicines restricted patient access?

When cancer medicines are available through insurance schemes, coverage or reimbursement in some settings may be subject to the patients or the medicine supply having met some pre-specified eligibility criteria (Fig. 4.10). These criteria often relate to: indications (e.g. conditions and line of treatment); patient characteristics (e.g. age, condition, prior treatments); qualifications of the physician (e.g. specialist only); and context of use (e.g. hospital only). The restrictions may be enforced as part of the “prior authorization” process (see Section 3.3.3) or through limiting supply only to approved physicians or facilities.

Fig. 4.10: Decision outcomes on the coverage of cancer medicines (2002–2014) in 10 European countries or areas



Source: (*148*)

The application of eligibility criteria is usually based on some clinical and economic rationales to ensure efficient and high-quality use of medicines by physicians or facilities that are most qualified for delivering the medicines, and for patients who are most likely to benefit from the treatment. However, some restrictions and system designs might limit patient access to essential treatments unnecessarily, to the extent that such measures might be deleterious to patients' health.

> *Applying eligibility criteria could ensure efficient and high-quality use of medicines, but some restrictions and system design might unduly limit patient access*

For example, a study that surveyed 450 haematologists and oncologists in Brazil, Mexico, Russia, Turkey and the USA[xiv] found that 61% of the survey participants considered the costs of rituximab as a barrier to patient access. The most common reasons cited by the surveyed physicians for cancelling, delaying, reducing treatment with rituximab were (1) insurance or government refused to fund the treatment (36%); (2) patients had no insurance or not eligible for reimbursement (29%); (3) patients were unable to pay co-payment (26%); and (4) hospital did not have the fund to provide rituximab (8%) (*279*). While further information is required to assess the appropriateness of the restriction, it appears that the restrictions on rituximab in these countries might have potentially caused worse health outcomes.

Another example is access to targeted therapy in Bosnia and Herzegovina. In this case, patients who required access to targeted therapies through the Solidarity Fund were often put on a waiting list. A study found that in 2005–2013, less than 10% of patients with chronic lymphocytic leukaemia and lymphoma in Bosnia and Herzegovina received treatment with rituximab within 3 to 4 months through the Solidarity Fund, while most patients on a waiting list had never received it (*280*). Similarly, the median waiting time for receiving treatment with imatinib among patients with chronic myeloid leukaemia or gastrointestinal stromal tumour in Bosnia and Herzegovina was 14 months (*280*). The delay in receiving imatinib for leukaemia might have had a negative impact on patient treatment outcomes, as suggested by surrogate measures: complete cytogenetic response[xv] after 12 months of therapy was achieved in 67% of patients who had immediate access to imatinib, compared to 18% and 15% of patients whose treatments were delayed by 6–12 months and more than 13 months while on the waiting list, respectively (*281*). Similarly, major molecular response rates[xvi] at 12 months occurred in 10% of patients who received immediate treatment, in contrast to 6% and 0% of patients who needed to wait for 6–12 months and more than 13 months to receive imatinib treatment, respectively (*281*).

Another example relates to the well-documented restrictions on patient access to hepatitis C medicines globally (e.g. sofosbuvir) because of their high unit costs and high demand. For example, a 2015 survey of reimbursement criteria of Medicaid's policies in 42 states in the USA found that (*282*):

- 74% (of the state policies) limited access to persons with advanced fibrosis or cirrhosis;
- 23.8% required persons co-infected with HCV and HIV to be receiving antiretroviral therapy or to have suppressed HIV RNA levels;
- 69% had restrictions based on prescriber type; and

[xiv] Survey date prior to 2014 but exact survey date was not noted in the published study.

[xv] A response measure of the number of genetic abnormalities (e.g. Philadelphia chromosomes) in the blood and bone marrow.

[xvi] A response measure when there is no or an extremely low level of abnormal genes (i.e. BCR-ABL gene) in the blood.

- 88% included drug or alcohol use in the eligibility criteria, with 50% requiring a period of abstinence and 64% requiring urine drug screening.

These highly restrictive requirements did not conform to clinical recommendations. The inconsistent requirements might have resulted in inequitable access and negatively affected patient health outcomes.

4.2.3 Judicious selection and rational application of access requirements

Notwithstanding, it must be emphasized that judicious selection of cancer medicines and rational application of access requirements with consideration to specific health system context can deliver better value for money for patients and the health care system, particularly for newer high-cost medicines of low clinical value (see Chapter 2). To demonstrate this point, the following case studies present comparative evidence on access to cancer medicines in New Zealand, Australia and the USA.

New Zealand has approximately 4.7 million people and the total government health care expenditure in 2015–2016 was around NZ$ 15 billion (US$ ≈11 billion) (*283*). Authorities in New Zealand are known to have adopted a restrictive approach for the listing and pricing of medicines to reflect the country's local context and health needs. As a result of the approach, studies have found that New Zealand has lower access in terms of the range of cancer medicines covered by public funding than in other countries (*284,285*). However, evidence suggests that the lower availability of cancer medicines has not had a negative impact on patient access to medicines that deliver good clinical value. To this point, a study compared publicly-funded cancer medicines in New Zealand and Australia to assess if there were any foregone population health gains as a result of unfunded cancer medicines in New Zealand (*286*). This study found that, as of April 30 2016, New Zealand funded 26 fewer cancer medicines than Australia. However, only six of these medicines/indications funded in Australia[xvii] delivered clinically meaningful overall survival gains, as defined by the American Society of Clinical Oncology guidance (*286*). Furthermore, clinicians in New Zealand would most probably have access to alternatives medicines for treating patients with the same type of cancers. The study therefore concluded that (*286*):

Judicious selection of cancer medicines and rational application of access requirements with consideration of specific health system contexts can improve patient access

> A policy of funding more new cancer medicines in order to achieve numerical parity with Australia or other countries would not result in substantive health improvement and would cost significantly more, and investing the millions of dollars needed to achieve funding parity with other countries would not represent good value for money in terms of delivering the best health outcomes for all New Zealanders, rather selective funding of new medicines that demonstrate clear clinical benefit and that are cost-effective and affordable is the sensible approach.

To further this point, despite being less restrictive than New Zealand, Australia – a country of about 24.5 million people with a government health care expenditure of AU$ 115 billion (US$ ≈90 billion) (*287*) – has also been noted as being more restrictive in providing access to cancer medicines than other countries (*284,285,288*). For example, a study compared access to 34 US FDA-approved cancer medicines in 2000–

[xvii] Cetuximab for head and neck cancer; cetuximab and panitumumab for colorectal cancer; pertuzumab and toremifene for breast cancer, trametinib for melanoma

2009 in the USA and Australia (*288*), and found that the Australian government's PBS provided coverage to only 12 medicines (35%) in 2010, many of which had restrictions such as pre-authorization, initiation requirements stricter than the approved (regulatory) label, and the application of continuation rules based on proof of treatment response (*288*). This is in contrast to the so-called unrestricted access in the USA through Medicare Part B and coverage of 93% of the 34 medicines in Medicare Part D (*288*). This study also found that the decision-making approach in Australia had led to delayed access: the average time between regulatory approval and coverage decision was 15.8 months (*288*). In the USA, while there was a delay between US FDA approval and assignment of insurance reimbursement codes of 16.3 months, patients could gain access to the medicines during the interim period, albeit within the context of potential unevenness in access due to a lack of clarity in reimbursement procedures (*288*). Notwithstanding this seemingly lower and delayed access to cancer medicines in New Zealand and Australia, broad epidemiological trends indicate that both New Zealand and Australia have comparable, if not superior, survival outcomes for patients with cancer than countries that have seemingly less restrictive access to cancer medicines, including the USA (*11*). These comparative case studies show that access to cancer medicines, while important, is only one part of the spectrum of cancer care required for improving the health outcomes of cancer patients.

KEY POINTS

- **Patients in countries with lower income had lower access to cancer medicines, with availability often subject to higher out-of-pocket payments by patients.** Access to a significant proportion of medicines listed on the EML (up to 57.7%) was subject to the patients incurring the full costs. The trend of lower availability in lower-income countries is particularly prominent for higher-cost medicines, including medicines that require genetic profiling.
- **Judicious selection of cancer medicines and rational application of access requirements with consideration of specific health system contexts can deliver better value for money without compromising population outcomes in cancer treatment**. A policy of funding more new cancer medicines to achieve the same number of cancer medicines as in other countries would not result in substantive health improvement and would cost more. However, there is evidence that in some countries, cost-containment measures due to the high costs of cancer medicines have caused reduced, delayed and even cancellation of treatment, to the extent that it might have deleterious impacts on patient health outcomes.

4.3 Impacts on affordability

Section 1.1.2 presents evidence that the expenditure on cancer medicines globally has been rising faster than the rate of growth in the number of cancer patients. Spending on cancer medicines has also outpaced the growth of the overall health care expenditure globally, particularly in regions with a large proportion of lower-income countries. Increased spending on cancer medicines is likely to be due to increased medicine prices because there has not been evidence to suggest a concurrent increase in the intensity of cancer treatment. As noted by numerous stakeholders, the prices of cancer medicines and the associated costs are not affordable to the health care systems globally in the long term.

When the cost of cancer medicines becomes unaffordable and unsustainable, health systems may be forced to restrict health expenditure by limiting demand and containing spending, as demonstrated in the examples described in Section 4.2.2. Indeed, evidence indicates that the demand for medicines from governments of low-income countries is particularly sensitive to changing prices (*143*). This means that when the prices of cancer medicines become higher, governments in low-income countries might reduce the supply of medicines, thereby compromising timely patient access to medicines. In the absence of sufficient insurance coverage, unaffordable prices have kept many cancer medicines out of reach of a large proportion of patients living with cancer. For example, oncologists in Pakistan were reluctant to prescribe biological cancer medicines because of their high costs: 96.7% of biologics were considered unaffordable because their monthly costs were higher than 20% of the monthly household's income after spending on food (*289*). For non-biological cancer medicines, only 58.1% were considered affordable in Pakistan (*289*).

> *When the cost of cancer medicines becomes unaffordable and unsustainable, health systems may be forced to restrict health expenditure by limiting demand and containing spending*

To assess the affordability, or the lack thereof, of cancer medicines at current prices, this report presents a three-step analysis undertaken according to the following hypothetical questions:

a) If countries were to spend 1% to 5% of their total annual health expenditure on cancer medicines with a view to providing universal coverage to these medicines, what would be the per-person "budget" for cancer medicines per year (see footnote on assumption[xviii])?

b) How would the size of this per-person budget for cancer medicines compare to the costs of common treatment regimens for various cancers?

c) In the absence of insurance coverage, what would be the duration of time that an individual would need to work in order to obtain sufficient income, from earning the average population wage, to pay for a course of treatment fully out of pocket?

For question (a), the analysis first multiplied the reported per-capita health expenditure in each country by the corresponding population estimates (*27,290*) to determine the total health expenditure. Based on the specified scenario, the analysis assumed 1–5% of the estimated total health expenditure being allocated to cancer medicines. The estimated total expenditure on cancer medicines was then divided by the number of new cases of cancer patients in each country (*291*) to determine the per-person budget, and presented by the World Bank's country and lending grouping[xix].

[xviii] The numerical values were assumed according to expenditure on pharmaceuticals and proportion of cancer-related disease burden. Firstly, countries might dedicate their total health expenditure to pharmaceuticals in proportion similar to the Member States of the OECD, which were between 6.6% and 28.8% in 2016 (see Appendix E). Of the expenditure on pharmaceuticals, countries might distribute resources to different disease areas in proportion to the distribution of disease burden. Based on the Global Burden of Disease Study, cancer accounted for 4% (low-income countries) to 17% (high-income countries) of the total disease burden in 2015, as measured by DALYs (see Appendix E). Thus, the analysis assumed that countries would spend between 0.3% (6.6% × 4%) and 4.9% (28.8% × 17%) of the total health expenditure on cancer medicines (alone). For simplicity, the analysis assumed 1% to 5%. These are **generous assumptions** because the proportions were calculated based on the upper limit, and spending on medicines for other disease areas may deliver larger health gains than from cancer medicines.

[xix] https://datahelpdesk.worldbank.org/knowledgebase/articles/906519

The analysis found that low-income countries could spend on average up to US$ 3800 per cancer patient annually on cancer medicines for all newly-diagnosed cancer patients, and the total expenditure on these medicines would be within the generously assumed 5% of the total health expenditure (Table 4.2). In high-income countries, the analysis found that a budget threshold of 5% of the total health expenditure would allow a spending of up to US$ 40 600 on cancer medicines per patient per year, with a view to providing universal coverage.

Table 4.2: Estimated annual expenditure on cancer medicines per patient by country income level

Expenditure threshold	1% total HE	2% total HE	3% total HE	4% total HE	5% total HE
Low income	$ 800 ($ 600; $ 1 000)	$ 1 500 ($ 1 200; $ 2 000)	$ 2 300 ($ 1 700; $ 3 000)	$ 3 000 ($ 2 300; $ 4 100)	$ 3 800 ($ 2 900; $ 5 100)
Lower-middle income	$ 1 600 ($ 1 100; $ 2 600)	$ 3 200 ($ 2 200; $ 5 200)	$ 4 800 ($ 3 300; $ 7 700)	$ 6 400 ($ 4 300; $ 10 300)	$ 8 000 ($ 5 400; $ 12 900)
Upper-middle income	$ 3 100 ($ 1 900; $ 4 500)	$ 6 200 ($ 3 800; $ 9 100)	$ 9 400 ($ 5 700; $ 13 600)	$ 12 500 ($ 7 500; $ 18 100)	$ 15 600 ($ 9 400; $ 22 600)
High income	$ 8 100 ($ 4 700; $ 14 600)	$ 16 300 ($ 9 400; $ 29 200)	$ 24 400 ($ 14 100; $ 43 800)	$ 32 500 ($ 18 800; $ 58 500)	$ 40 600 ($ 23 500; $ 73 100)

Note: HE = health expenditure. Numbers represent median US$ in 2016, with interquartile ranges in parentheses

Source: Author's calculations based on (*27,290,291*)

For question (b), Table 4.3 (p.78) shows the estimated annual costs of standard treatment regimens for a select set of cancers, calculated based on the dosages recommended in clinical guidelines and the prices of cancer medicines in India, South Africa, Australia and the USA. These countries were selected to illustrate prices of medicines in countries of different economies and with different levels of price regulations. The analysis found that the estimated treatment costs frequently exceeded the per-patient annual "budgets" estimated in question (a), despite the generous assumptions of 1% to 5% of total health budget being spent on cancer medicines (alone). For example, the treatment cost for one patient with chronic myeloid leukaemia for a year would be between US$ 800 and US$ 96 700 for imatinib and US$ 800 to US$ 109 400 for dasatinib, which are higher than the per-person budget of US$ 800 to US$ 40 600 estimated in Table 4.2. The unaffordability was even more prominent when considering the standard treatment regimen for early stage HER2-positive breast cancer, where the estimated costs ranged between US$ 18 500 and US$ 71 000. These examples suggest that, at current prices, universal coverage of cancer medicines (alone) will greatly exceed 5% of total expenditure on health care. This is unaffordable and unsustainable.

> *The estimated costs of cancer treatment frequently exceed the estimated per-patient annual "budgets" even if countries were to spend 1% to 5% of their total annual health expenditure on cancer medicines to provide universal coverage of cancer medicines*

Table 4.3: Estimated costs of cancer pharmacotherapies, by cancer type and country

Cancer	Standard regimen[a]	Estimated annual cost of cancer medicines[b] Nominal value[c] (with adjustment for purchasing power)			
		India	South Africa	Australia	USA
Breast cancer Early stage HER2 positive	doxorubicin, cyclophosphamide, docetaxel, trastuzumab [Adjuvant AC-TH]	$ 18 500 ($ 67 900)	$ 33 900 ($ 74 400)	$ 41 800 ($ 37 000)	$ 71 700 ($ 71 700)
Colon cancer Stage III	capecitabine, oxaliplatin [Adjuvant CAPOX or XELOX]	$ 2 200 ($ 8 100)	$ 1 300 ($ 2 900)	$ 1 200 ($ 1 000)	$ 7 300 ($ 7 300)
Liver cancer Advanced	sorafenib	$ 700 ($ 2 700)	$ 12 700 ($ 27 800)	$ 28 700 ($ 25 400)	$ 90 800 ($ 90 800)
Prostate cancer Castration-sensitive metastatic	goserelin, bicalutamide docetaxel [ADT plus DOCE]	$ 3 600 ($ 13 300)	$ 3 300 ($ 7 200)	$ 4 100 ($ 3 600)	$ 7 100 ($ 7 100)
Lung cancer Metastatic non-small cell	vinorelbine, cisplatin	$ 1 800 ($ 6 600)	$ 800 ($ 1 900)	$ 1 200 ($ 1 000)	$ 500 ($ 500)
	erlotinib for EGFR positive	$ 1 700 ($ 6 200)	$ 27 300 ($ 59 800)	$ 13 400 ($ 11 900)	$ 76 700 ($ 76 700)
Lymphoma Non-Hodgkin – diffuse large B-cell	rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone [R-CHOP21]	$ 6 700 ($ 24 600)	$ 20 000 ($ 43 900)	$ 17 800 ($ 15 700)	$ 48 100 ($ 48 100)
Leukaemia Chronic myeloid	imatinib	$ 800 ($ 2 800)	$ 13 300 ($ 29 100)	$ 23 200 ($ 20 600)	$ 96 700 ($ 96 700)
	dasatinib	$ 800 ($ 3 100)	$ 20 000 ($ 43 800)	$ 40 200 ($ 35 600)	$ 109 400 ($ 109 400)

Note: [a] Please refer to the WHO Essential Medicines List and clinical guidance for specific details of the treatment regimens.
[b] Costs were estimated for a full course or 12-month treatment. Cost calculations were based on body surface area of 1.8 m^2 or body weight of 75 kg where necessary. Please note that the cost estimates are indicative only. [c] Numbers represent US$ in 2016.
Source: Regimens *(292,293)*; Prices in India *(294,295)*, South Africa *(296)*, Australia *(297)*, USA *(298)*; exchange rates *(237)*

In the absence of financial support from governments, the treatment costs presented in Table 4.3 would not be affordable to individual patients. For example, a course of standard (adjuvant) treatment for early stage HER2 positive breast cancer (Adjuvant AC-TH) would cost about 10 years of average annual wages in India and South Africa, and 1.7 years in the USA[xx]. Patients with non-Hodgkin lymphoma in India, South Africa and the USA would require, respectively, 3.7 years, 5.6 years and 1.1 years of wages to cover for the costs of a standard course of treatment (R-CHOP). In general, standard courses of treatment are more affordable in Australia compared to the other countries.

[xx] Assuming weekly wages (i.e. not disposable income) of ₹ 2 250 in India, R 910 in South Africa and US$ 827 in the USA based on official sources.

It is important to note that while some treatment regimens seem more affordable (e.g. for Stage III colon cancer), chemotherapy was intended as an add-on therapy following surgical intervention (e.g. removal of section of the colon with the cancer along with nearby lymph nodes). This means that the costs of chemotherapy would add significantly to the financial burden in patients who do not have adequate financial protection from public or private insurance. Furthermore, the estimated costs do not include costs associated with supportive care (e.g. anti-emetics and haematopoietic growth factors), which are often essential for the safe delivery of the treatment. Finally, while the nominal treatment costs are lower in lower-income countries, the treatment costs exceeded the estimated costs in higher-income countries when purchasing power was taken into consideration (estimates shown in parenthesis in Table 4.3). This shows that cancer medicines were comparatively more expensive in lower-income countries after accounting for purchasing power.

> *Treatment would not be affordable for individual patients without financial support from governments*

Even with the support of an insurance scheme, patients often suffer financial hardship directly attributable to the high cost of cancer treatment, particularly with new so-called targeted cancer medicines. For example, a 2014–2015 survey in the USA sought to assess the financial situation of patients with multiple myeloma who were insured and had received at least three months of ongoing treatment (*299*). It found that 36 (36%) of the 99 respondents reported having applied for financial assistance and 21 (21%) having borrowed money to pay for medicines (*299*). Financial distress among insured cancer patients was also reported in other studies in the USA (*300–302*), and other high-income countries such as Singapore (*303*) and France (*304*). In Iran (*305*) and India (*306*), studies showed that financial hardship was common among general cancer populations.

> *Patients often report financial hardship directly attributable to the high cost of cancer treatment, even with the support from an insurance scheme*

There is evidence that financial distress may adversely affect patient health outcomes. For example, a regression analysis in the USA found that cancer patients who filed for bankruptcy had 79% higher risk of deaths compared to their counterparts who were comparable except for not having filed for bankruptcy (*307*). When under financial stress, cancer patients may take less medicines than prescribed, fill a partial prescription, or even forego treatment, as shown in a study in the USA (*308*). Government policies could help mitigate the financial risks of patients, with possible effects on the psychological well-being of individual patients (*309*). However, it is important to ensure that any progress in minimizing patient out-of-pocket costs is not being offset by the rising prices of cancer medicines. For example, in the USA, rising prices of targeted oral cancer medicines between 2007 and 2017 has gradually eroded the Government's effort in closing the coverage gap (*310*).

Finally, with the number of people living with cancer predicted to grow in the coming decades, the unaffordability of cancer medicines will only worsen if the current price trend continues. Considering the range of evidence suggesting the unaffordability of cancer medicines, governments and stakeholders globally should consider implementing policies to correct the current high prices.

KEY POINTS

- **Expenditure trend on cancer medicines suggests that prices of cancer medicines are not affordable by health care systems globally**: The expenditure on cancer medicines globally has been growing faster than the growth rate in the number of cancer patients. Spending on cancer medicines has also outpaced the growth of the overall health care expenditure globally, particularly in regions with a large proportion of lower-income countries. Despite the steep increase in spending on cancer medicines, the availability of cancer medicines remains low in many countries.
- **Universal coverage of cancer medicines (alone), at current prices, would greatly exceed a generously-assumed budget of 5% of total health care expenditure.** At current prices, standard treatment regimens for a select set of cancers would cost much more than the estimated annual per-patient "budget" of US$ 800 to US$ 40 600, calculated based on the generous assumption that 1% to 5% of total health care expenditure would be spent on cancer medicines alone.
- **In the absence of insurance coverage, cancer treatments would be unaffordable to a large proportion of patients**. For example, a course of standard treatment for early stage HER2 positive breast cancer would cost about 10 years of average annual wages in India and South Africa, and 1.7 years in the USA. The costs associated with other interventions (e.g. surgical interventions and radiotherapy) and supportive care (e.g. anti-emetics and haematopoietic growth factors) would worsen the unaffordability of the overall care. Even with insurance coverage, patients in many countries have reported experiencing financial stress, to the extent that they would lower the treatment dose, partially fill a prescription or even forego treatment altogether to mitigate the costs.

4.4 Impacts on research and development

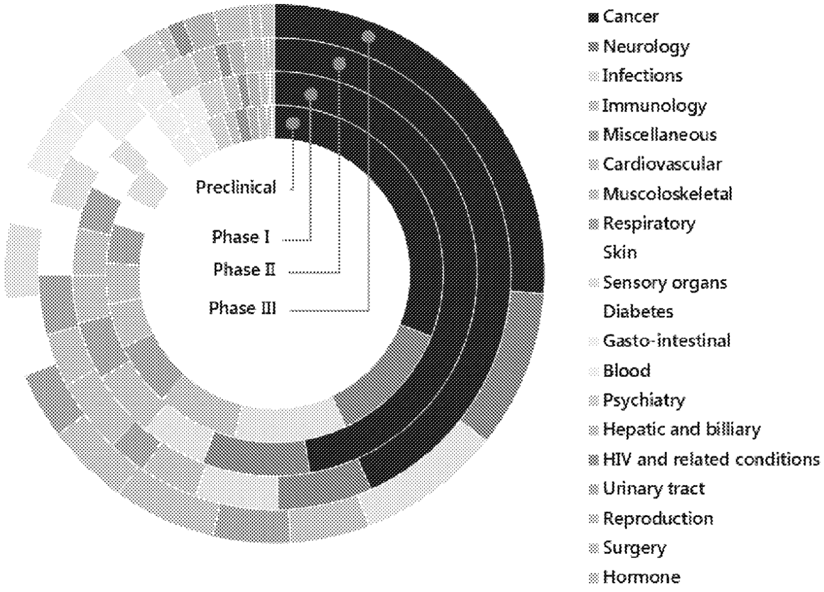
4.4.1 R&D efficiency and innovation

One viewpoint often put forth to defend the high prices of cancer medicines is the need for rewarding innovation to incentivize R&D of future medicines. This argument would be true only insofar as the financial reward is insufficient. As presented in Section 3.2.1.5 (p.23) and noted by other commentators (*311*,*312*), returns from cancer medicines, through high prices, are much higher than what would be considered a fair return in economic terms. That is, the returns on the factors of production of cancer medicines are in excess of what would be necessary to maintain operation of the pharmaceutical industry. As suggested by economic theory, excessive returns, combined with market dominance (Section 3.2.2.2), could encourage companies to engage in wasteful rent-seeking activities such as lobbying and filing patent clusters to delay entry of generic/biosimilar products (Section 4.1.5), distort investment and stifle innovation. Indeed, the past and present trend of R&D for cancer medicines has observed some of these potential consequences, discussed below.

> *Excessive financial returns, combined with market dominance could encourage companies to engage in wasteful rent-seeking activities (e.g. lobbying and filing patent clusters to delay entry of generic/biosimilar products), distort investment and stifle innovation*

Firstly, there is evidence of seemingly disproportionate levels of research for cancer medicines. A study found that the number of pharmaceutical clinical trials in cancer (4006) was far higher than the number of clinical trials in other therapeutic areas such as neurology (726), communicable diseases (556), immunology (436) and cardiovascular disease (446) (Fig. 4.11, p. 81) (*313*). Such high level of investment (46.6% of all trials) seems counter-intuitive considering the oft-cited lower success rates of clinical trials for cancer medicines (7% likelihood of marketing approval from Phase I compared to up to 18% for non-cancer medicines) (*314*) and the highest number of discontinued projects (*315*). In other words, economic rational reasoning would have diverted the pharmaceutical industry away from, not towards, the R&D of cancer medicines in order to minimize the possibility of lost investment. The higher level of investment in the R&D of cancer medicines might be explained by the considerable financial incentives in place to safeguard the higher risks of failure. Therefore, it could be argued that the high financial returns from cancer medicines, together with other government's incentives (Section 4.4.2), might have over-incentivized the pharmaceutical industry to dedicate considerably higher, possibly disproportionate, levels of investment towards the R&D of cancer medicines.

Fig. 4.11: Distribution of pharmaceutical preclinical and clinical trials in 2016, by disease



Source: (313)

Secondly, the high level of investment on R&D of cancer medicines would have been more than desirable if it were to produce medicines with clinically meaningful benefits, particularly when cancer is one of the most complex public health challenges of our time (Section 1.1.1). While there have been some encouraging successes, several leading experts in cancer research have pointed out the considerable inefficiency in the current R&D of cancer medicines. These experts are concerned that such inefficiencies would jeopardize innovation of cancer medicines in the long term.

For example, an assessment of a large global clinical trial registry (ClinicalTrials.gov) in 2016 found that there were 803 clinical trials on testing checkpoint immune-therapeutics undertaken by 14 pharmaceutical companies (*316*). This represented about one-fifth of all clinical trials on cancer medicines (*313*). The total planned enrolment for these trials was over 166 000 trial participants. This total sample size represents a large number of patients, considering that patients would need to meet eligibility criteria and give consent, and that most trial participants would live in higher-income countries (*316*). The competition for enrolling patients with similar characteristics might lengthen the duration of trial and reduce the overall productivity of clinical trials. The duplication of research effort is not unique for checkpoint immune-therapeutics. Indeed, another study found a significant duplication of research effort across the cancer R&D portfolio, with 124 (74%) of the 172 oncology agents in the pipelines from nine major pharmaceutical companies in 2014 having an overlapping mechanism of action (*69*).

In response to the duplication of research effort for checkpoint immune-therapeutics, the heads of major research centres in the United Kingdom, USA and the Netherlands commented (*33*):

> There is enormous redundancy in these studies, as many pharmaceutical companies perform similar trials with comparable drugs, but fail to share the data generated. This herd mentality is caused in part by the notion that immune checkpoint therapies can indeed lead to long-lasting remissions (potentially even to cures) and that significant numbers of patients in each clinical indication benefit from these treatments. While it is in the short-term good that so many patients get access to potentially lifesaving drugs, in the longer term, patients will have to pay the price for this inefficiency and duplication.

Similarly, the chief editor of a major medical journal commented when reflecting on the vast oncology literature reviewed by the editorial team (*317*):

> Trial redundancy [in oncology] is blatantly evident; frequently two or more trials are performed in similar patient cohorts, with both studies asking the same basic research question, and with the same agents being tested. However, quite often these trials do not arrive at the same conclusion or fail to provide a definitive, practice-changing outcome.

The inefficiency of R&D for cancer medicines not only relates to duplication, but also a counterproductive ethos of pursuing marginal indications. For example, a study showed that only 30 (42%) of the 71 cancer medicines approved by the US FDA between 2002 and 2004 could be considered as having "clinically meaningful improvements" according to ASCO's Value Framework (*69*). In other words, of the so-called successful medicines, many only demonstrated marginal benefits compared to the available treatments. In other cases, there was limited progress following extensive investment in time and resources (e.g. the decade-long clinical trial programme for bevacizumab and pemetrexed for the treatment of metastatic colorectal cancer and (non-mutated) non-small cell lung cancer, respectively) (*69*). Experts have also highlighted that some failed investment in the R&D of cancer medicines could have been prevented. For example, 25 cancer medicines targeting a part of cell division (mitosis) went into an extensive programme of clinical trials despite the fact that there was no compelling prior evidence of efficacy in humans for these medicines (*69*). As a result, the multibillion-dollar investment only resulted in a response rate of approximately 1% in more than 2000 solid tumours (*69*).

The inefficiency of R&D for cancer medicines not only relates to duplication, but also a counterproductive ethos of pursuing marginal indications

In summary, the number of clinical trials on cancer medicines is significantly higher than in other therapeutic areas, but there is evidence of inefficiencies from research duplication and the pursuit of marginal benefits. The inefficiencies and distortion of investment could be due to excessive returns from cancer medicines combined with market dominance. This might put long-term innovation of cancer medicines at risk.

4.4.2 Incentives for investment in research and development on cancer medicines

Some stakeholders, including the industry, have expressed concerns that attempts to lower medicine prices might impair the incentives for R&D of cancer medicines. However, evidence suggests that *at this point in time and for cancer medicines*, lowering medicine prices would not impair the incentives for R&D of cancer medicines.

Firstly, as in Section 3.2.1.5, the costs of R&D (and production) may bear little or no relationship to how pharmaceutical companies set prices for cancer medicines. In fact, evidence suggests that linking R&D costs to the prices of medicines, after accounting for public contributions towards drug discovery, would see a sizeable reduction in the prices of many cancer medicines. Secondly, at present, the financial returns from cancer medicines are high, to the extent that the returns could distort investment and stifle innovation (Sections 4.4.1). *At this point in time and for cancer medicines*, lowering current prices might in fact be conducive to long-term innovation. Further incentives through an alternative financing scheme might be helpful but not be instrumental in stimulating innovation in the sector. Thirdly, financial return is a function of price and volume; potential impact on revenue due to lower prices could be offset by higher volume, particularly when the marginal cost of production is low (Section 3.2.1.2). Finally, it is important to recognize that financial return is only one of the ways to incentivize R&D activities; governments globally have made significant contributions to incentivize the discovery of medicines, both financially and non-financially.

Indeed, the public sector has made a wide range of contributions towards the R&D of medicines, spanning from providing direct funding for undertaking basic science research and clinical trials, building physical research infrastructure (e.g. synchrotron and laboratories), to supporting the operation of institutions (e.g. cancer registries). Governments' contributions also include building generations of medical research workforce through education programmes. Excluding infrastructure investment and labour development, public sector investments in health R&D accounted for 30% of the total US$ 240 billion funding globally in 2009 (*318*). The remaining 60% of R&D investment came from the business sector and 10% from non-profit-making organizations (*318*).

Public sector, publicly funded academic institutions and non-profit-making organizations have made a wide range of contributions towards the R&D of medicines

A specific example of public sector contribution towards drug discovery is the considerable scaling-up of genome programmes globally (*319,320*). These projects have received funding largely from governments or philanthropic organizations (e.g. The Wellcome Trust) and have markedly accelerated biomedical research by leading to better understanding of genetic variation in humans. The outputs from these projects have served as the backbone of drug discovery and driver for innovations. These include most notably in the development of so-called targeted or precision cancer medicines over the past decades (*321*).

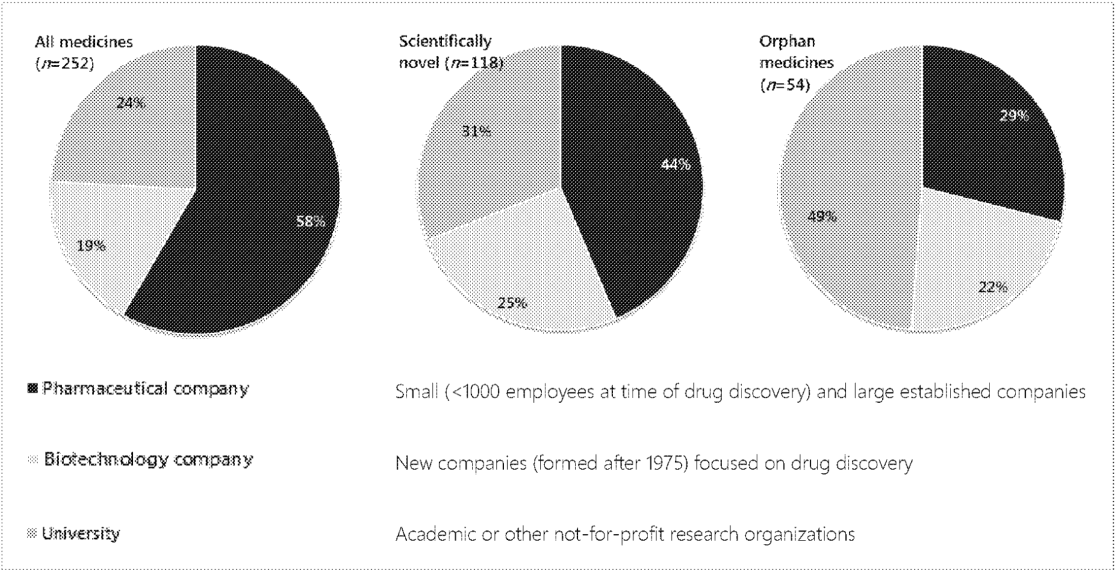
Drug discovery efforts in the private sector would not be possible without the concurrent contributions from governments, and by extension tax-payers

It could be argued that many of the drug discovery efforts in the private sector would not be possible without the concurrent contributions from governments, and by extension tax-payers. Indeed, a study found that funding from the United States National Institutes of Health (NIH) of US$ >100 billion over more than 200 000 grant-years has contributed to every one of the 210 new medicines approved by the US FDA in 2010–2016 (*322*). There is also evidence that public sector investment has had positive knock-on effects on the private sector (i.e. positive externalities). For example, a study found that NIH funding in the USA stimulated the development of private-sector patents at approximately 2.3 patents for an additional US$ 10 million in NIH funding (*323*). In the United Kingdom, medical research funded by the Government and charities had increased as well alongside private sector R&D, suggesting the synergistic nature of R&D (*324*).

In addition to financial support, publicly-funded academic institutions and non-profit-making organizations have also played a direct and significant role in drug discovery. For example, a study found that about one in four US FDA-approved medicines from 1998 to 2007 originated from academic and non-profit-making organizations (Fig. 4.12). The proportions of medicines originated from academic and non-profit-making organizations increased to 31% and 49% for scientifically novel and orphan medicines (*325*).

One in four US FDA-approved medicines from 1998 to 2007 originated from academic and non-profit-making

Fig. 4.12: Distribution of medicines approved by the US FDA from 1998 to 2007, by sector



Source: (*325*)

In cancer, there are numerous examples of public sector investment leading to the discovery of medicines. Table 4.4 presents examples where the public sector has played a significant role in the discovery of cancer medicines. Other examples noted in the literature, but not presented in the table below, include imatinib (*326*), palbociclib (*327*), HPV vaccines (*328*), trastuzumab, alemtuzumab, CAR-T therapies (*329*), cabazitaxel, radium-223 and olaparib (*330*).

Table 4.4: R&D pathways and public and private sources of funding for cancer medicines

Medicine	R&D milestones	R&D funding source[a]	Financials
Abiraterone (*331,332*)	**1980s–1990s:** The Institute of Cancer Research (ICR) in the United Kingdom investigated inhibition of the production of male sex hormones through inhibiting enzyme CYP17 **1992**: ICR filed patents on abiraterone **1993**: Abiraterone entered the licensing portfolio of Cancer Research UK **1996**: ICR assigned rights for the development of abiraterone to British Technology Group, which out-licensed to Boehringer Ingelheim, but was later returned to British Technology Group due to concerns of possible side-effects **2004**: Abiraterone was licensed to Cougar Biotech. **2009**: Johnson and Johnson announced acquisition of Cougar Biotech for US$ 1 billion **2011**: Regulatory approvals of abiraterone	**Public/non-profit-making** Cancer Research UK Medical Research Council **Private** British Technology Group; Boehringer Ingelheim; Cougar Biotechnology; Janssen (Johnson & Johnson)	Royalty to Cancer Research UK: US$ 1.7 billion in 2013 Cumulative revenue to 2017: US$ 12.2 billion (nominal)
Temozolomide (*333*)	**1987:** Discovery of temozolomide **1992–1997**: Results from Phase I and Phase II trials **1992**: Cancer Research UK licensed Schering-Plough (later acquired by Merck in 2009) **1999**: EU Commission granted marketing authorization **2005**: US FDA approval of temozolomide	**Public/non-profit-making** Cancer Research Campaign (formed part of Cancer Research UK in 2002) Cancer Research UK Aston University University of Strathclyde **Private** Schering Plough/Merck	Payment to Cancer Research UK: US$ 5.5 million + royalty of up to US$ 20 million per year Cumulative revenue 2017: US$ 12.4 billion
Sofosbuvir (*334*)	**1990s**: Development of subgenomic replicon to enable testing of antiviral compounds **2001–2008**: Apath, LLC, through multiple grants from the NIH, commercialized the replicon **2001–2006**: Pharmasset received multiple grants from NIH and the Veterans Health Administration **2007–2015**: See Fig. 3.3 (p.23)	**Public/non-profit-making** NIH; Veterans Health Administration **Private** Pharmasset Gilead	Gilead bought Pharmasset for US$ 11 billion Cumulative revenue: US$ 50.1 billion (nominal)
Enzalutamide (*335–337*)	**1990s–2004**: Researchers from University of California, Los Angeles (UCLA) studied the role of androgen receptor in advanced prostate cancer **2005**: UCLA filled patents on enzalutamide and licensed to a biopharmaceutical company – Medivation **2009**: Medivation entered worldwide agreement to co-develop and co-commercialize enzalutamide **2007–2010**: Medivation ran Phase I–III clinical trials **2012**: US FDA approved enzalutamide **2016**: Royalty Pharma acquired rights to a portion of the future royalties co-owned by UCLA, 8 UCLA researchers, and Howard Hughes Medical Institute **2016**: Pfizer bought Medivation for US$ 14 billion	**Public/Non-profit-making** UCLA; Howard Hughes Medical Institute; NIH; U.S. Department of Defense (Prostate Cancer Research Program); Prostate Cancer Foundation **Private** Medivation Astellas Pharma	Royalty to UCLA, UCLA researchers and Howard Hughes Medical Institute: US$ 1.14 billion Cumulative revenue to 2017: US$ 713.9 million

Note: [a] May not be exhaustive

In addition to providing direct contribution towards the discovery of medical research, governments in many countries have also implemented a range of indirect measures to incentivize R&D. These include allowing private companies to claim high-level tax credits or deductions for activities related to R&D (Table 4.5).

Table 4.5: R&D incentives for pharmaceutical companies and clinical research organizations

Jurisdiction	Structure	Level	Jurisdiction	Structure	Level
Australia	Credit	40% to 45%	**Russian Federation**	Deduction	4% to 150%
Brazil	Deduction	160% to 180%	**Singapore**	Deduction	50% to 300%
Canada	Credit	15% to 35%	**South Africa**	Deduction	150%
China	Deduction	150%	**Republic of Korea**	Credit	7% to 50%
India	Deduction	100% to 200%	**Turkey**	Deduction	50% to 100%
Japan	Credit	5% to 30%	**United Kingdom**	Credit/ deduction	11% to 225%
Netherlands	Deduction	5% to 160%	**United States**	Credit	14% to 20%

Note: Tax credit provides a direct reduction of income tax liability. Tax deduction lowers the taxable income, which may result in the final taxable income being in a tax bracket with a lower tax rate.

Source: (*338,339*)

In summary, public and non-profit-making sectors, and by extension tax-payers and philanthropists, have provided considerable financial and non-financial contributions towards the R&D of cancer medicines. This means that in many cases, pharmaceutical companies have not incurred the full costs of R&D. The pharmaceutical industry has also benefited greatly from the knowledge generated by public-sector investments in R&D, and by having access to research supported by public funding at costs, if any, lower than the market value.

> *Some stakeholders have questioned whether companies could claim to recover the full costs of R&D through setting high prices for medicines*

Considering these facts, some stakeholders have questioned whether pharmaceutical companies could claim to recover the full costs of R&D through setting high prices for medicines (*340,341*). More directly, these stakeholders are seeking clarity as to whether the public has been "paying twice", or should be paying twice, for the hundreds of medicines developed at least with partial support from public resources (*340*). This raises an important question: does the public have the right to expect governments to play a greater role in exercising more stringent pricing regulations, or simply, by imposing lower prices for cancer medicines in order to realize a more direct financial return for public investment on behalf of the tax-payers? Another pertinent question is whether the ongoing push by government policies to commercialize research outputs from publicly-funded universities have tilted the risk–benefit balance in favour of the pharmaceutical industry at the expense of the tax-payers (*342*). Furthermore, it is important to clarify the relationship between the government, industry and university when pursuing joint research ventures (*343*).

There are no simple answers to these issues as they require alignments in laws, competition policies, industrial development policies and governance of the knowledge economy. Furthermore, it would be highly challenging to operationalize a pricing approach that would accurately account for public contribution for the R&D of cancer medicines. Notwithstanding, these are important topics that warrant open debates, so as to find mutually agreeable solutions that could potentially lead to more affordable medicine prices.

4.4.3 Financing gaps for research and development on cancer

Determining the financing gaps for R&D on cancer medicines and other cancer care requires an assessment of what ought to be the "right" level of R&D investment and activities in different areas. This is not a question easily answered because it involves technical assessments that are complex and often flawed with methodological shortcomings. It also involves value judgments about the areas society sees as the priorities. For these reasons and as discussed below, whether a research area is "over-" or "under-funded", and hence the financing gaps for research, would require consideration from multiple perspectives.

Determining financing gaps for cancer R&D requires both complex technical assessments as well as value judgments about what society sees as the priorities

On the technical side, it is difficult to find an objective benchmark to indicate whether the level of R&D investment and activities in a particular area of cancer care is appropriate. A group of benchmarks that have been commonly used for assessing research priorities and gaps relate to various measures of disease burden. These include prevalence, mortality, and years lived with disability (*344–347*). For example, a systematic review of public and philanthropic funding to all cancer research institutions in the United Kingdom from 2000 to 2013 found that research funding had not been allocated according to the relative disease burden (*344*). On this basis, the study suggested possible "underinvestment" in the research for cancers of the liver, thyroid, lung, oesophagus, stomach and bladder, because these cancers collectively accounted for 47.9% of deaths from all cancers globally, 44.3% of disability-adjusted life years and 20.4% of years lived with disability (*344*). In contrast, the study found that haematological, breast and prostate cancers received the highest proportions of funding in terms of number of awards (26.9%, 13.3%, 2.1%, respectively) and sum of funding (16.0%, 5.8%, 5.7%) (*344*). On this basis, the study suggested that haematological, breast and prostate cancers were "relatively well-funded" in the United Kingdom (*344*). These findings are similar to previous studies (*346,347*). In fact, previous studies went as far as noting that the relative spending on leukaemia in the United Kingdom was "quite extreme" (*346*) and breast cancer appeared to be "overfunded" because the funding had increased despite a reduction in years of life lost over 2002–2012 (*347*). Studies from the USA and Canada also observed similar findings regarding the higher proportional allocation of funding towards leukaemia and breast cancers, and considerable underfunding in cancers of the lung and pancreas (*345,348*). Based on these findings, authors from one of the studies suggested that "shifting resources from those cancers that are overfunded to those that are underfunded may increase the overall efficiency of cancer research with respect to reducing societal burden" (*347*).

Drug therapies have received considerably higher proportions of funding in number and amount compared to radiotherapy and surgical interventions

Another benchmark for assessing the appropriateness of funding level is by the types of interventions. For example, the above-mentioned systematic review on public funding for cancer research institutions in the United Kingdom found that drug therapies received considerably higher proportions of funding in number and amount (25.7% and 26.0% of total number of awards and funding amount) (*344*). This is compared to the low level of funding for radiotherapy (2.6% and 3.7%) and surgical interventions (1.7% and 1.6%) (*344*). Similarly, a cross-sectional analysis of trials registered on a trial registry – ClinicalTrials.gov – in the decade from June 2007 confirmed this trend. It found only 1 378 (5.3%) among the 25 907 identified oncological trials to be related to radiotherapy, suggesting an underinvestment because radiotherapy is important in the clinical management of cancer (*349*). The study also found that there were lower numbers of industry-sponsored clinical trials in radiotherapy (5.8%) compared to other oncological trials (43.4%) (*349*).

Looking more broadly across all disease areas, it could be argued that funding directed towards research in cancer could be considered disproportionately high. As shown in Fig. 4.11 (p.81), trials on cancer medicines have dominated the overall portfolio of preclinical and clinical trials on pharmaceuticals, to the extent that these cancer trials might have displaced research resources for other disease areas with higher disease burden[xxi]. Of course, this assertion would be true only if one were to accept disease burden as the sole basis for allocating research funding. Indeed, the assumption that allocation of research funding for each type of cancer should be proportional to their respective disease burden has been challenged (*350*). Similar to the debate on whether burden of disease should guide priority setting for health services (*351*), there are at least three weaknesses in using disease burden as the primary benchmark for distributing research resources.

- Disease burden would direct priorities according to the size of the problem, rather than what would be the most efficient and equitable use of resources: From an economic perspective, directing resources towards areas with the higher likelihood of "doing good" should be the guiding principle (*351*). For example, it has been noted that temozolomide and bevacizumab were the only two medicines approved for cancers of the central nervous system since 1999 despite "more than 70,000 individuals in the USA being diagnosed with a primary brain malignancy and 151,669–286,486 suffering from metastatic CNS cancer in 1999" (*352*). Logically and based on disease burden, more resources should be dedicated towards drug discovery for the central nervous system (CNS) programme. However, dedicating more resources might not be sensible because stakeholders have identified a range of barriers that would not be mitigated by simply having more resources (*352*).
- A large proportion of cancer research is not specific to an anatomical site: Many research programmes in cancer are not site-specific. For example, more than half of all cancer research funding in Canada was not site specific (*350*). Disease-oriented allocation of funding does not reflect the operational aspects of cancer research in reality and would therefore lead to underinvestment of non-site-specific research.
- Disease burden methodology only "measures the measurable": The methodology of burden of disease does not include assessment of social value, such as community's perceived duty and proclivity for helping people in greater need. For example, allocating resources according to disease burden would not encourage research for rare and neglected cancers. It might also divert resources away from cancers more prevalent in resource-poor settings (e.g. liver cancers, Kaposi sarcoma, Burkitt lymphoma).

[xxi] Diseases with the highest DALYs: cardiovascular disease; diarrhoea; lower respiratory and other infectious disease. Diseases with the highest years lived with disability: mental disorders; musculoskeletal disorders; etc. (*297*)

On the last point above, society may have preference and prejudices against certain cancers (i.e. value judgement). For example, it has been noted that underfunding in the research for cancer of the lung may be related to low awareness about lung cancer or social stigma against smokers. In contrast, leukaemia and breast cancer seemed to be overfunded because of higher level of awareness and societal preference for helping children and young mothers (*345,347*). The higher level of funding in leukaemia and breast cancer areas may therefore be in line with social expectation, and hence, be justified.

Higher funding levels in leukaemia and breast cancer areas may be in line with social expectation, and hence, be justified

In summary, it is challenging to judge if there are gaps for R&D on cancer medicines without a comprehensive assessment of what ought to be the "right" level of R&D for different types of cancers, considering a range of factors such as disease burden, existing therapies and social expectations. With these caveats, research suggests that research for haematological and breast cancers might be overfunded, while research for cancers of the liver, thyroid, lung, oesophagus, stomach, bladder and pancreas might be underfunded.

KEY POINTS

- **The high financial returns from cancer medicines gained through high prices might have distorted research investment and stifled innovation**. The number of pharmaceutical clinical trials in cancer was far higher than in other therapeutic areas. This suggests that the financial returns from cancer medicines and other government incentives have at least mitigated the high failure rates for cancer medicines R&D. In fact, the excess financial returns and other government incentives might have over-incentivized the pharmaceutical industry, which has led the industry to dedicate a considerably higher, possibly disproportionate, level of investment for the R&D of cancer medicines, many of which are redundant and only aimed for achieving marginal benefits.
- **At this point in time and for cancer medicines, the concerns that lower medicine prices might impair future R&D might be misplaced** because (1) prices of cancer medicines bear little or no relationship with R&D costs (i.e. no observable linkage between prices and R&D costs); (2) financial returns from cancer medicines are high; (3) potential impact on revenue due to lower prices could be offset by higher volume, especially when the marginal cost of production is low; (4) governments and the non-profit-making sector have made substantial contributions to the R&D of medicines through direct funding and other incentives such as R&D tax credits or reductions.
- **Determining research priority and gaps require both technical assessment and value judgment.** Studies suggested that research for haematological and breast cancers might be overfunded, while research for cancers of the liver, thyroid, lung, oesophagus, stomach, bladder and pancreas might be underfunded. However, these studies assumed that allocation of research funding for each type of cancer should be in proportion to their respective disease burden, which has been and could be challenged.

4.5 Impacts on price and pricing transparency

4.5.1 Rebates and discounts have impaired price transparency

As discussed in Section 0, over the past decade, many payers globally have entered into MEAs with pharmaceutical companies to enable patient access to medicines under certain conditions, of which, discounts and rebates are the most common provisions in these agreements (Fig. 3.10, p.42). Newer cancer medicines are most commonly subject to these agreements because of their high prices and uncertain clinical benefits (*192,193*). In other jurisdictions (e.g. the USA), rebates or discounts may be offered directly to consumers through coupons and vouchers, or to intermediaries such as wholesalers, pharmacy benefit managers and clinical service institutions (*48,353*).

The use of discounts and rebates may signal competition in the market and is often considered a legitimate competitive practice if applied within the boundaries of laws. However, the terms and conditions of these agreements are often confidential. The confidential terms include non-disclosure of the discounts and rebates, rendering the net transaction prices of medicines between the sellers (e.g. manufacturers, service providers) and the payers (governments, consumers) opaque. This lack of price transparency and its possible impacts on access to affordable medicines has been a recurrent point of discussion in the debate on medicine prices, discussed below.

The use of discounts and rebates may signal competition in the market, but a lack of price transparency and its possible impacts on access to medicines have been debated

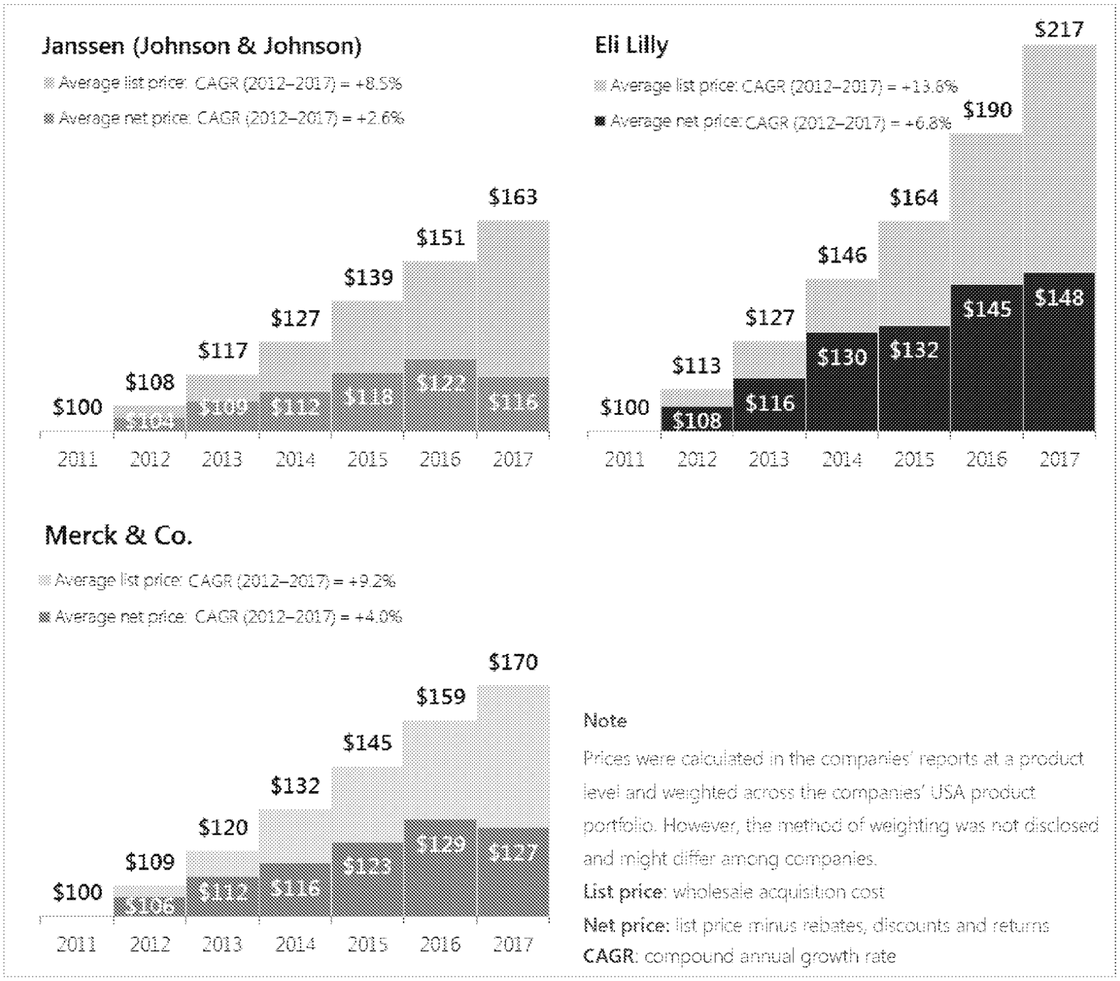
4.5.2 Magnitude of rebates and discounts

In general, the level of discount or rebate for medicines has been noted to be below 50% of the list price (*354*). In recent years, in response to the growing concerns about rising medicine prices in the USA, three pharmaceutical companies have disclosed aggregated pricing information by presenting changes in the average list prices and changes in the average net prices across the product portfolio in the USA (*355–357*). To illustrate the differences in list and net prices from 2012 to 2017, Fig. 4.13 presents the changes in price by applying the year-on-year percentage changes reported by these companies to a hypothetical medicine with a net price of US$ 100 in 2012. As shown, both the average list prices and the average net prices have increased from 2012 to 2017 for the three companies. The compound annual growth rates were higher for the average list prices between 8.5% and 13.8%, while the average net prices grew between 2.6% and 6.8%. As a result of the different rates of growth, Fig. 4.13 also shows the growing differences in the average list prices and net prices. This suggests possible increase in the magnitude of the rebates or discounts (although the change could also be influenced by the changing mix of products).

Growing differences in list prices and net transaction prices of medicines (i.e. after discount and rebates) may be perceived as an industry's strategy to mask the true increases in medicine price

Disclosure of pricing information from these companies does improve transparency regarding the *overall* magnitude of rebates or discounts. However, these highly aggregated figures do not allow the authorities or the informed public to better understand the companies' pricing practices, let alone to judge if such practices were responsible or not (*357*). In fact, the growing gaps between the list prices and net prices might invite a perception that the industry has been pushing medicine prices higher by factoring in a higher level of discounts, with a view to masking the true price increases at the level of individual medicines.

Fig. 4.13: Cumulative changes in the average list price and average net price from 2012 to 2017 for a US$ 100 medicine in 2011, in the United States



Note

Prices were calculated in the companies' reports at a product level and weighted across the companies' USA product portfolio. However, the method of weighting was not disclosed and might differ among companies.

List price: wholesale acquisition cost

Net price: list price minus rebates, discounts and returns

CAGR: compound annual growth rate

Source: Author's calculations based on percentage year-on-year price changes presented in (355–357)

4.5.3 Possible motivations of confidential rebates and discounts

A pertinent question is what motivates pharmaceutical companies and payers to engage in such practice. First, like other businesses, pharmaceutical companies have a natural tendency in keeping their prices and discounts undisclosed. In general, businesses would try to articulate or influence the unique value of their medicines in order to lead the buyers to accept the proposed prices as well justified (Sections 3.2.1.3 and 3.2.2.2). Confidential discounts or rebates allow the list prices to remain high in preparation for future negotiations with potential buyers, while facilitating listing of the medicines with a lower net price. In some health care systems, the discounted price might even help the medicine being prioritized in drug formulary as the "preferred medicine" to prescribe. Furthermore, pharmaceutical companies may use undisclosed discounts to apply price discrimination, that is, selling the

> *Companies have a natural tendency in keeping their prices and discounts undisclosed*

same medicine at different prices according to the payers' willingness to pay, with a view to maximizing profits (Section 3.2.2.3). This may create unfairness as the differences in prices may not correlate with countries' ability to pay for the medicines, or other measures of equity. Finally, confidential agreements also prevent competing companies from knowing the exact pricing strategy.

> *Absence of full information and the difficulties in mandating disclosure of costs and prices have diminished the usefulness of cost-based and external referencing pricing*

On the other hand, any diligent payers would naturally want to know how the pharmaceutical companies had arrived at the proposed price in order to ensure that the offer is reasonable. As discussed in Section 3.3, payers may set a price by allowing the company to add a mutually agreeable level of mark-up on top of the costs through cost-based pricing; or try to benchmark the offer against the prices in other countries through external reference pricing. However, there is considerable paucity in the costs of R&D and production because of the proprietary nature of the information (Section 3.2.1). The absence of full information and the difficulties in mandating disclosure essentially diminish the usefulness of cost-based pricing for setting medicine price. The confidential nature of the agreements also impairs the effectiveness of external reference pricing because only the list prices are visible in the market. In fact, the use of external reference pricing may be inflationary in the long term because it "motivate(s) pharmaceutical companies to keep list prices high" (p.144) (*109*). Notwithstanding, in addition to achieving better prices and faster patent access, payers have noted the following rationales for entering confidential agreements (*354*):

- volume- or expenditure-based rebates provide budgetary predictability
- outcome-based rebates address clinical uncertainty about health outcomes
- parallel export of medicines can be prevented
- outcome-based rebates link drug pricing to performance more clearly.

4.5.4 Possible impacts of lacking price transparency

4.5.4.1 Theoretical arguments

At a conceptual level, a lack of price transparency is not consistent with the notion of good governance and contravenes the principles of economic theory in enhancing market efficiency.

The principles of good governance demand that the process leading to change and the outcomes derived therefrom should be accountable, transparent, abide the rule of law, responsive to the needs of the community in a timely and appropriate manner, fair and inclusive, effective and efficient, as well as participatory and consensus-oriented (*358*). By not disclosing the terms and conditions of MEAs, tax-payers, or at least well-informed stakeholders, would not be in a position to participate in decision-making and judge if the responsible authorities have acted in the best interest of tax-payers or not. This could potentially compromise clear lines of accountability – a commonly espoused objective of national medicines policies (Section 3.1, p.16). A lack of price and process transparency may even lead to corruption, especially in health care systems with weak overall governance (*359*).

> *A lack of price transparency is inconsistent with the notion of good governance and may impair market efficiency*

From the perspective of conventional economic theory, confidential pricing arrangements mask market pricing structures and create informational asymmetry – a known condition for causing market failure. Economic theory suggests that one of the conditions to achieve an efficient market is to ensure that both parties of a transaction have all relevant information to make the best decision from their respective positions. If all other conditions for a competitive market were to be met and all other things equal, pricing transparency would enhance efficiency by promoting price competition. However, in the medicine markets, the imbalance of power in transactions is common, where multinational pharmaceutical companies have more information on prices, and even information on the benefits and harms of medicines during price negotiation, than the party negotiating on behalf of national, regional, or individual health care authorities. In wanting to achieve access to new medicines for their patients and in the absence of full information, purchasing parties reportedly felt "pressurised" into accepting the offers and conditions proposed by pharmaceutical companies, despite having insufficient information to be confident if a favourable deal or offer had been achieved or not (*360*). This suggests that confidential agreements might result in inefficient outcomes from an economic perspective.

> *Purchasing parties reportedly felt "pressurised" into accepting offers and conditions proposed by pharmaceutical companies, despite having insufficient information to be confident in making an informed*

In contrast, theoretical arguments have been presented to contend that, under some conditions, price transparency can lead to adverse outcomes, including "increase prices paid by the poor, deter business entry in poor markets, reduce competition, lower investment, and mislead if inaccurately measured by a third party" (*361*). The crux of the argument is that increasing price transparency might cause pharmaceutical companies to apply uniform pricing for all buyers in order to avoid the appearance of unfair pricing. On the assumption that profit-maximizing pharmaceutical companies would be "more likely to set low prices in developing countries and high prices in developed countries", a uniform price would likely be "between the firm's preferred price in developed countries and that in developing countries" (p.1386) (*361*). This would, in turn, "harm people in the developing countries". The paper also argued that, at worst, the companies might "elect not to sell to buyers in low-price markets", and that uniform pricing might "facilitate collusion among sellers" and make "cartels easier to enforce" (*361*), on the assumption that regulators are ineffective in identifying large-scale illegal business practices.

> *It seems a clear remiss of duty for society and governments to put so much responsibility in private companies to apply differential pricing for medicines at their discretion to achieve socially-desirable outcomes*

While informative from a theoretical viewpoint, the assumptions underlying the arguments could be challenged. For example, there is no evidence to show that profit-maximizing pharmaceutical companies would be more likely to set low prices in developing countries and high prices in developed countries. On the contrary, as shown in Sections 4.1.4 and 4.1.2, there is evidence that prices of medicines are highly dispersed and poorly correlated with the country's ability to pay, as demonstrated by the observed prices of cancer medicines and hepatitis C medicines, particularly in middle-income countries (*144*). Furthermore, as shown in Section 4.2, pharmaceutical companies seem to have already chosen not to launch or delayed the launch of medicines in countries with lower capacity to pay, irrespective of whether prices were disclosed or not. Finally, it seems a clear remiss of duty for society and governments to put so much responsibility in private companies to apply differential pricing at their discretion to achieve socially-desirable outcomes, when the raison d'être of these companies, as required by the law at least at this point in time, is to fulfil the fiduciary duty to maximize shareholder return rather than maximizing social impact.

4.5.4.2 Evidence on the effectiveness of confidential agreements

By default, there is a dearth of evidence on the effectiveness of these confidential agreements. This report only identified one survey of authorities from public or social health insurance systems in 11 countries or areas: Australia, Austria, Canada, England, Scotland, Germany, the Netherlands, New Zealand, Norway, Sweden and the USA (U.S. Department of Veterans Affairs) (*354*). The most commonly reported benefits from survey respondents was the ability to obtain better prices for patented medicines than published manufacturers' prices (*354*). This observation was expected given the very intent of negotiation and agreement structure. Most respondents perceived the confidential discounts as being "very beneficial" or "somewhat beneficial" (*n*=7) to their local health system, while acknowledging that confidential discounts could be "somewhat or very detrimental" (*n*=4) to health systems worldwide (*354*). It is questionable if these contrasting perceptions could simultaneously be correct, considering that none of the respondents had information about the prices in other health systems.

> *It is unknown if confidential agreements have achieved lower medicine prices and faster access than would be otherwise achieved*

Indeed, it is unknown if these agreements have lowered the prices of medicines more than would be otherwise achieved in the absence of confidential provisions. It is also unknown if health care systems had in fact achieved faster access to medicines for patients than would be otherwise achieved if these agreements were not confidential. Even if faster patient access had been achieved, it would be prudent from the perspective of good governance to understand the extent to which any trade-offs had been made in achieving these goals, including the administrative burden of negotiating and executing the agreements. Arguably, the widespread adoption of these agreements might have perpetuated the imbalance of information and negotiating powers between payers and manufacturers.

4.5.4.3 Evidence on the effectiveness of transparency measures

There is also limited context-specific empirical evidence to indicate that improving price transparency leads to better price and expenditure outcomes. For example, WHO's Vaccine Product, Price and Procurement (V3P) Project aims to provide middle-income countries with "accurate, reliable and neutral vaccine product price and procurement data, to improve forecasting, budgeting and sustainable financing of vaccines" (*362*). It only presented self-reported qualitative information to show that favourable outcomes have been achieved through greater price transparency, such as better contract negotiations, and price reduction resulting in savings in some countries (e.g. Countries in the WHO Western Pacific Region, and Indonesia, Lebanon) (*362*). In Brazil, the Government implemented a programme – Banco de Preços em Saúde – that mandated publication of purchasing prices on the ministry of health's website for all federally funded hospitals with ≥320 beds. The purposes are to facilitate the centralization of pricing information, and to decrease the high cost of

> *It is also unknown if improving price transparency would lead to better price and expenditure outcomes*

medicines and medical supplies (*363*). A regression analysis showed that there was no consistent pattern of decreasing prices within the two Brazilian states during the five-year period for which the prices were analysed, with 5 out of 191 (non-cancer) medicines showing price decrease in one state and none in another state (*363*).

KEY POINTS

- **Increased use of confidential rebates and discounts have impaired price transparency**: The use of discounts and rebates may signal competition in the market and is often considered a legitimate competitive practice if applied within the boundaries of laws. However, the proliferation of confidential agreements on rebates and discounts to facilitate faster access to high-cost medicines, including cancer medicines with uncertain clinical benefits, have masked market transparency, including the level of price competition.
- **Growing differences in list price and net transaction price may invite distrust and may impair the effectiveness of external reference pricing**: The industry may be perceived as pushing medicine prices higher by factoring in a higher level of discounts, with a view of masking the true increases in medicine price, particularly at the level of individual medicines. Pharmaceutical companies may also be motivated to keep list prices high to impair the effectiveness of external reference pricing.
- **A lack of price transparency is not consistent with the notion of good governance**: Confidential agreements may compromise clear lines of accountability – a commonly espoused objective of national medicines policies. A lack of price and process transparency may even lead to corruption, especially in health care systems with weak overall governance.
- **Theoretical arguments regarding the effect of price transparency are equivocal**: Conventional economic theory indicates that price transparency would enhance efficiency. In contrast, it has been argued that increasing price transparency might cause price convergence towards the mean, potentially making lower-income countries worse off. However, both arguments are based on debatable assumptions, given the complexity of the health care market.
- **By default, there is a dearth of evidence on the effectiveness of these confidential agreements**: While perceived as beneficial by most authorities from public or social health insurance systems, it is unknown if these agreements have in fact lowered the prices of medicines and improved patient access to medicines than would be otherwise achieved in the absence of confidential provisions.
- **On the other hand, there is limited context-specific empirical evidence to indicate that improving price transparency leads to better price and expenditure outcomes**: Further research is needed to monitor the impact of improving price transparency.

4.6 Unintended negative consequences

This section considers possible negative policy outcomes that have deviated from the original policy intent. Some of these observed consequences are considered "unintended" as they were unplanned from the policy perspective. Other consequences are clearly objectionable as they contravene the law.

4.6.1 Indication expansion in cancer medicines initially designated with orphan drug status

4.6.1.1 Context

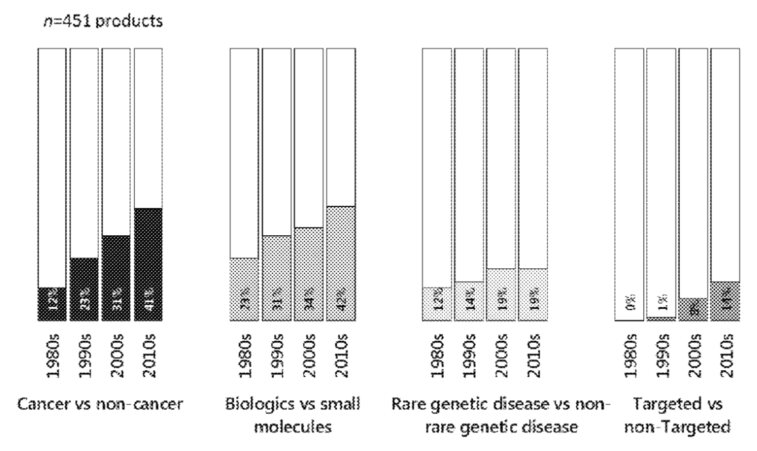
The advancement in biological science over the past decades has led to more detailed characterization of disease, leading to identification of rare diseases and rare variants of common disease, as well as potential opportunities for developing medicines targeting specific molecular alterations (*364*). Given its pathogenesis and pathophysiology, cancer has been one of the areas where this trend is most noticeable (Section 2.1).

> *Governments have implemented a range of policy incentives to stimulate the R&D of medicines for rare diseases, including rare cancers*

Governments have implemented a range of policy incentives to stimulate the R&D of medicines for rare diseases. For example, the United States Government enacted the Orphan Drug Act in 1983 to encourage the development of medicines for rare conditions: rare diseases as those affecting "less than 200,000 persons in the United States", or more than 200 000 persons, but for whom "there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will be recovered from the sale in the United States" (*365*). The Act offers (1) seven years of market exclusivity from the date of US FDA approval; (2) potential research grants of up to US$ 14 million per year; and (3) 50% R&D tax credit (compared to the existing 14–20% tax credit for R&D) (*366*). Since December 1999, the European Union has also enacted legislation to grant orphan medicines 10 years of market exclusivity from the date of market authorization (*367,368*). There are also other incentives, including protocol assistance, regulatory fee reductions and potential research grants (*367*).

Together with the advancement of biological science, these incentives seem to have increased the number of orphan drugs approved by regulatory bodies. For example, US FDA has approved more than 600 orphan indications from more than 450 distinct medicines since 1983, compared to 10 industry-sponsored products for rare diseases 10 years prior to the enactment of the Orphan Drug Act (*369*). In cancer, there was a significant increase in the proportion of medicines approved for rare cancer, rising from 12% in the 1980s to 41% in the 2010s (Fig. 4.14). Between the 1980s and 2010s, there were also considerable increases in the proportions of biological medicines (from 23% to 42%) and targeted medicines (0% to 14%) (Fig. 4.14).

Fig. 4.14: Proportion of US FDA-approved orphan drugs 1983–2016, by decade and category



Note: Coloured proportions refer to the first categories: cancer, biologics, rare genetic disease and targeted therapy.

Source: (370)

> *Medicines for orphan diseases, despite smaller patient populations, have the commercial potential to generate revenue for the originator companies at least as great as for non-orphan medicines*

There is evidence to indicate that medicines for orphan diseases, despite having much smaller patient populations, have the commercial potential to generate revenue for the originator companies at least as great as for non-orphan medicines (*371*,*372*). One study, for example, found that at least 9% of orphan drugs "have reached blockbuster status" because revenue was greater than US$ 1 billion (*373*). Furthermore, the revenue would translate into higher profit for the companies because of (1) lower R&D costs due to government tax incentives, smaller clinical trial sizes, usually shorter duration of clinical trial; (2) higher rates of regulatory success and shorter approval time (*374*); and (3) longer period of market exclusivity (*371*). Furthermore, orphan drugs typically command high prices despite having modest efficacy at best. The high prices are often justified or accepted based on severe disease and small population affected due to rarity. Indeed, studies have found that payers in seven European countries – France, Germany, Italy, Norway, Spain, Sweden and the United Kingdom – appeared to value rarity in pricing decisions, as indicated by the inverse relationship between annual treatment costs and prevalence of the disease (*372*,*375*).

4.6.1.2 Possible unintended consequence

In view of these observations, there have been concerns that current R&D incentives, regulatory flexibility and pricing practices for orphan drugs might have unintendedly led companies to pursue an orphan indication in the first instance then expand to other non-rare indications. The strategy is to gain faster market entry at high prices (*365*,*376*). A review by the US FDA showed that 26% of 374 medicines initially approved as an orphan drug from 1983 to 2016 expanded their label to other indication(s) in the same rare disease (11%), other rare disease (8%) or non-rare disease (7%) (*369*). This study did not present the analysis specific for cancer medicines, but another preliminary study of the same US FDA dataset (2005–2015) found that cancer medicines accounted for 57% of 30 medicines that had expanded their indications from an initial orphan indication (*377*).

> *Current R&D incentives, regulatory flexibility and pricing practices for orphan drugs might have unintendedly led companies to pursue an orphan indication in the first instance then expand to other non-rare indications*

Furthermore, some cancer medicines with orphan designations have total patient populations greater than the threshold value (e.g. 200 000 patients per year in USA) across all approved indications. For example, bevacizumab and rituximab have received rare disease designations for four and seven rare-disease indications, despite having five and three non-rare disease indications (*369*). It raises a question about the numerical definition of rare disease and whether some cancer subtypes should be considered as rare disease, especially when pharmaceutical companies are known to engage in the "practice of salami slicing" to produce "artificial rare disease" (*365*,*376*). Furthermore, would the high proportion of R&D on rare cancer divert limited research resources away from other previously unaddressed or under-addressed rare diseases, as originally intended by initiating the government interventions to correct the undersupply of R&D for rare diseases? Finally, considering the high prices of medicines for rare diseases, how should pricing approaches best respond to the increasing number of cancer medicines with orphan designation to maintain the affordability of these medicines to the health care system and patients?

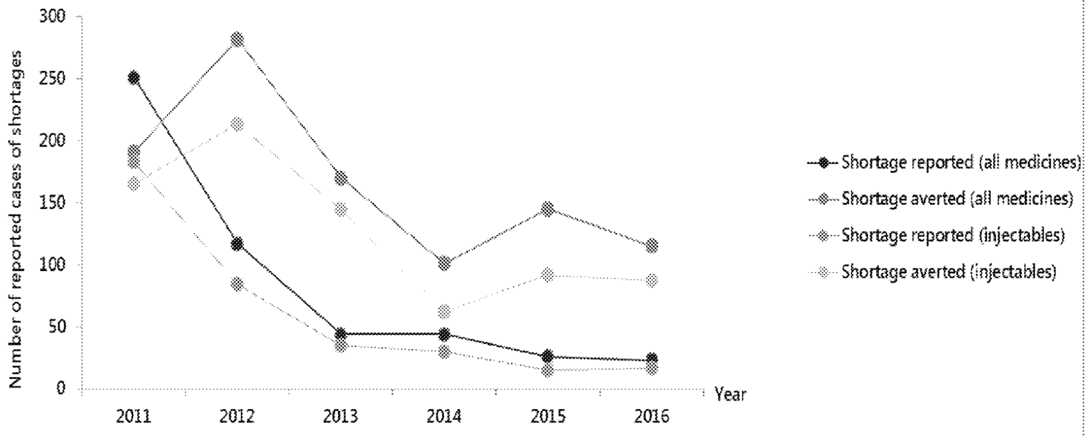
Actions have been initiated to address some of these questions (e.g. re-aligning the purpose of the programme (*378*) or to propose a pricing approach for medicines with orphan indications (*379*)). It is important to continue to monitor the trend in the use of orphan designation for cancer medicines, and when necessary adapt pricing approaches to ensure the sustainability of health care systems.

4.6.2 Shortage of cancer medicines due to low prices

4.6.2.1 Context

In recent years, the supplies of some cancer medicines have been disrupted, causing shortages (*380–385*). The true extent of shortages of cancer medicines, including the frequency and duration, is not clear. In terms of frequency, there is evidence showing that the overall number of shortages for all medicines has decreased in recent years, at least in the USA, with the US FDA having averted a significant proportion of medicine shortages (Fig. 4.15). Furthermore, injectable medicines account for a significant proportion of the reported shortages (Fig. 4.15). It is probable that shortages in cancer medicines correlated with the fact that many cancer medicines were formulated in injectable form, as injectable medicines were more susceptible to experiencing shortages due to their more complex manufacturing requirements (*380*,*383*,*385*).

Fig. 4.15: Number of cases of shortages reported to US FDA (2011–2016), by category



Source: (*383*)

This report did not identify robust information regarding the persistence of shortages, including for cancer medicines. It is also uncertain if cancer medicines were more commonly affected by shortages than medicines in other therapeutic areas. In a survey of European hospitals, cancer medicines was the second most commonly reported category of medicines affected by shortages (54.5% of respondents), after antimicrobial agents (56.7%) but higher than medicines for emergency (30%), cardiovascular disease (30%) and anaesthesia (26%) (*381*). In contrast, a review of literature and database in Europe showed that cancer medicines accounted for 12% of all reported medicines in shortage, lower than nervous system medicines (17%), antimicrobial agents (15%) and medicines for cardiovascular disease (14%) (*380*). These inconsistent estimates highlight the difficulties regarding data collection and interpretation in this area of research (*384*), because shortage is often time and location specific.

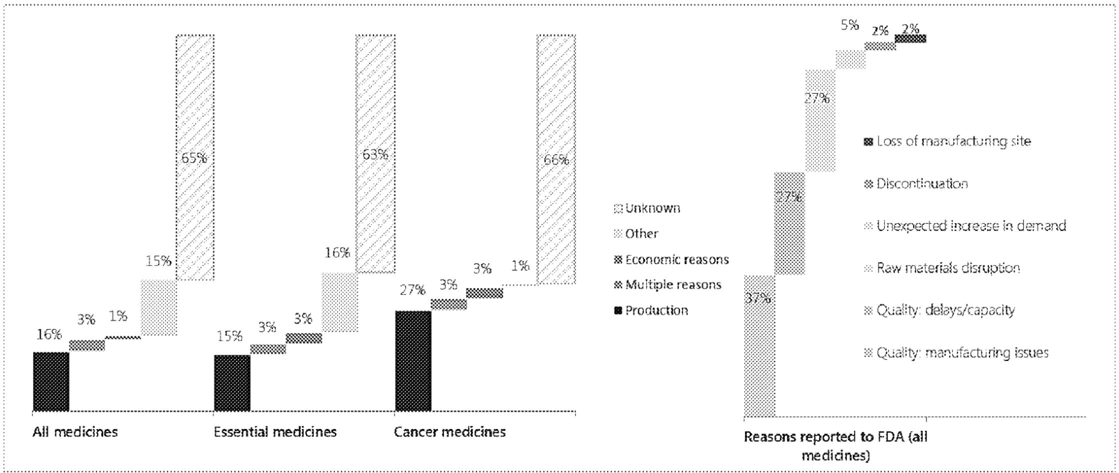
4.6.2.2 Possible unintended consequence

Causes of medicine shortages are complex and involve factors from both the supply- and demand-sides (*384,386*). "Economic reasons" has been noted as one of contributing factors towards shortages. It has been argued that manufacturers have much less incentive to ensure the ongoing supply of medicines with low prices. In paediatric cancer, the lack of a broader adult market for the medicines (e.g. actinomycin, mercaptopurine, thioguanine, asparaginase) or its particular paediatric formulations might also have diminished the overall market attractiveness. Furthermore, suppliers would divert medicines from countries with relatively low prices of medicines to countries with higher prices through parallel trade, thereby impacting on the supply of medicines in the former. Based on these reasons, it has been noted that shortages of cancer medicines could be an unintended consequence of pricing policy or contractual arrangement that seeks to achieve the lowest prices.

While economic reasons are worth noting, data from regulatory reporting indicated that, of the shortages with known reasons, most of the shortages resulted from problems related to production quality (Fig. 4.16). In lower-income countries such as Botswana and Romania, disruption of supply for cancer medicines were related to factors such as inadequate funding allocation, inefficient procurement practices and lack of robust method for predicting demand (*382,387*).

> *Most of the medicine shortages with known reasons resulted from problems related to production quality, rather than economic reasons*

Fig. 4.16: Causes of shortages reported to national reporting systems in Europe (2010–2013) and US FDA (2011–2016)



Source: (380,383)

It is acknowledged that there could be underreporting of economic reasons as a cause for shortage. However, until more compelling evidence is presented about the extent of shortages in cancer medicines or when there is a real susceptibility of supply disruption due to unsustainable prices, payers should not be deterred from seeking a lower price for fear of causing shortages. Even if low prices were associated with shortages, payers should give equal importance to reducing high

> *Payers should not be deterred from seeking a lower price for cancer medicines for fear of causing shortages*

prices as well as raising unsustainable low prices. This is so that the overall pricing would minimize the relative disincentive for the suppliers to prioritize higher priced and more profitable medicines over lower ones. Finally, as noted in Section 3.3.1.4, criteria and contract terms other than price (e.g. ability to supply) should be considered when evaluating the merit of a tender. This would avoid drug shortages caused by the sole winning tenderers' inability or unwillingness to supply due to lower profitability (*384*).

4.6.3 Inefficient, unethical and illegal conducts

High prices and profits from cancer medicines may encourage companies or individuals to take risks and engage in unethical, even illegal business practices. Some of the examples of these behaviours are documented below.

- Emergence of substandard or falsified medicines: In 2012–2013, the US FDA published on its website and sent safety notifications directly to physicians and clinics about the detection of falsified bevacizumab (Avastin) in the USA. The investigation has led to criminal prosecutions of domestic and international suppliers, physicians, a pharmacist, and clinic staff, who continued to purchase and supply falsified products despite having been alerted about the safety concerns (*388*). A geospatial and regression analysis of the location of falsified bevacizumab products, using the destination of US FDA safety notifications as a proxy, found that "individuals in counties where patients have greater ability to afford more expensive treatment, and consequently where providers can seek higher reimbursement, may have been at higher risk to counterfeit Avastin exposure" (*389*). Indeed, the criminal investigation has discovered that the primary motivation for illegal conduct was to secure lower prices to generate higher profits. The study asserted that the underlying problem leading to market demand for the falsified medicine was the general lack of affordability and accessibility to cancer medicines[xxii] (*388*). It could also be argued that the lack of price transparency and the need to seek a higher level of discounts and rebates might have also led to the emergence of substandard and falsified products. Furthermore, shortages of essential cancer medicines may also subject the health system to risks of substandard and falsified cancer medicines because patients might resort to sourcing medicines from unauthorized channels (e.g. shortages of 5-fluorouracil, asparaginase, vinblastine, methotrexate in Romania (*390*)). This case study shows the importance of ensuring affordable medicine prices and maintaining price transparency in order to avoid the emergence of substandard or falsified medicines.
- Anti-competitive business practices: In addition to anti-competitive business practices outlined in Section 4.1.5, companies may engage in business practices to delay competition, some of which violate the current antitrust laws in various jurisdictions. For example, in order to delay the entry of generic or biosimilar competition, the originator companies may replace a medicine nearing the end of market exclusivity period with a product of the same medicine that is covered under secondary patents on slightly modified features such as coating, salt moiety, formulation or method of administration. Originator companies may also misuse the requirements under the regulatory and patent systems to extend their market exclusivity. These include restricting generic manufacturers' access to the medicine so as to prevent bioequivalence testing – a mandatory regulatory requirement (*391*). Finally, pharmaceutical companies may abuse their monopoly power and engage in excessive price increase. For example, the European antitrust regulator is currently investigating a company for withholding the

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[xxii] Falsified and unauthorized products have also been detected for other cancer treatments, including rituximab, pegfilgrastim, zoledronic acid, oxaliplatin and gemcitabine.

supply of five cancer medicines where there were no alternatives – chlorambucil, melphalan, mercaptopurine, tioguanine and busulfan – after an authority in Spain declined to accept the company's demand for price increase of up to 4000%. The company had also engaged in similar business practice in Italy (*126,392*).

- Deceptive marketing activities: In 2006, Schering-Plough pleaded guilty and reached a settlement with the United States Department of Justice for concealing the price of temozolomide, promoting its off-label use and paying "illegal remuneration" to doctors to induce the utilization of temozolomide (*393*). In 2016, Genentech and OSI Pharmaceuticals paid US$ 67 million to resolve allegations of misleading claims about the effectiveness of erlotinib in a subgroup of patients with non-small cell lung cancer, when there was limited evidence to show that erlotinib was effective to treat this group of patients unless they also had never smoked or had a mutation in their epidermal growth factor receptor (*394*). In 2017, Celgene settled with the US Department of Justice for promoting thalidomide and lenalidomide for a broader range of cancers than approved, or prior to approval, by the US FDA. The allegations also include Celgene paying kickbacks to physicians to induce them to prescribe the drugs (*395*).

- Imposing wastage: There have been allegations that pharmaceutical companies have produced cancer medicines at pack sizes or dosages that would result in wastage. An analysis of 20 cancer medicines with the highest revenue in 2016 estimated that US$ 1.8 billion (10%) of the revenue was from discarded drugs because of the unused portions in the dosage presentation (*396*). For example, the manufacturer of pembrolizumab discontinued and replaced the supply of 50 mg vials with 100 mg vials in the USA in 2015, but the smaller, more flexible and cheaper dosage form of the 50 mg vial was later made available in Europe. These examples show that pharmaceutical companies may create inefficiencies with a view to maximizing profits.

KEY POINTS

- **Possible misalignment of incentives might have resulted in an increasing number of cancer medicines with orphan designation**: There is evidence to suggest that current R&D incentives, regulatory flexibility and pricing practices for orphan drugs might have unintendedly led pharmaceutical companies to pursue an orphan indication in the first instance then expand to other non-rare indications, with a view to gaining faster market entry at high prices.
- **Evidence of low prices causing shortages of cancer medicines is limited**: Evidence suggests that shortages in cancer medicines observed in recent years is probably due to problems related to the manufacturing of medicines formulated as injections, rather than due to economic reasons (e.g. less financial incentives to ensure the ongoing supply of medicines with low prices, or diversion of medicines from countries with relatively low prices of medicines to countries with higher prices through parallel trade). Until more compelling evidence is presented, payers should not be deterred from seeking lower prices for fear of causing shortages. This will minimize the incentive for suppliers to prioritize higher-priced and more profitable medicines over lower-priced medicines.
- **There are some documented examples of inefficient, unethical and illegal conduct induced by high prices or profitability of cancer medicines**: These include the emergence of substandard or falsified cancer medicines, antitrust practices, deceptive marketing activities for off-label prescribing and imposing wastage.

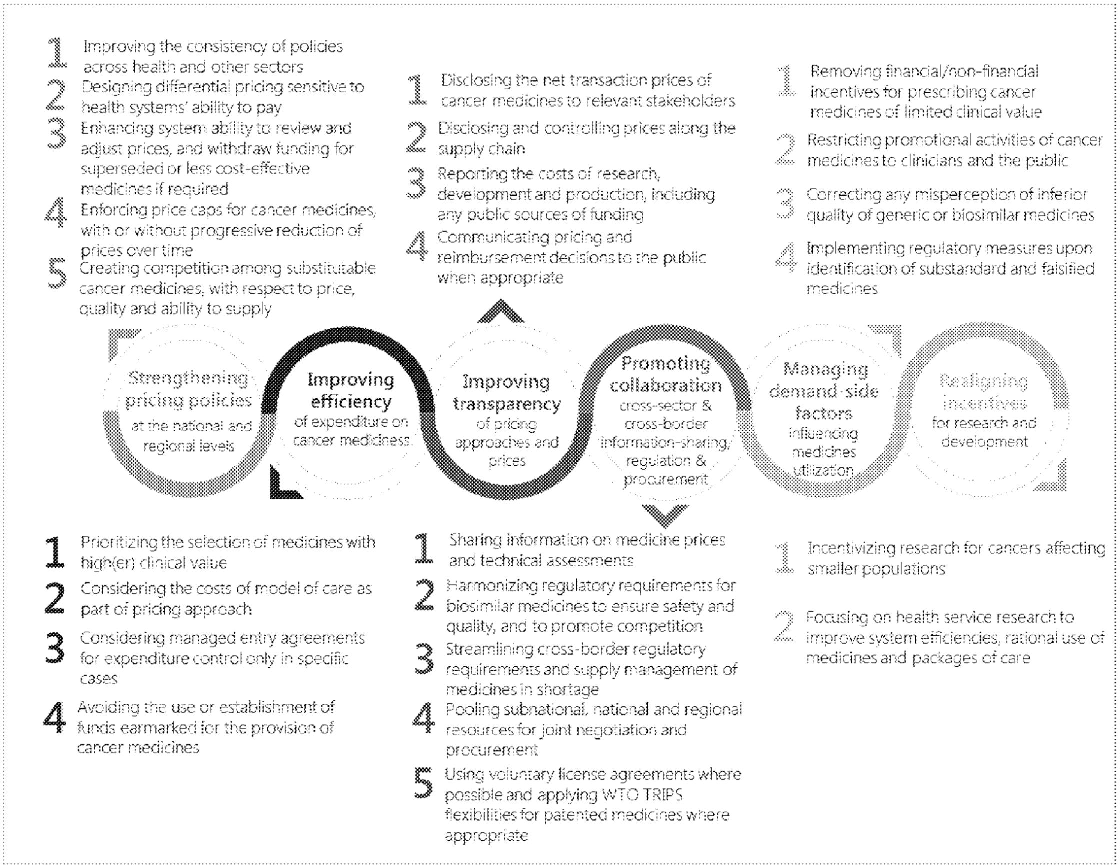
4.7 Summary

This chapter draws attention to how pricing approaches and policies, or the lack thereof, can have an impact on the prices, availability and affordability of cancer medicines, as summarized in the respective sections. It also shows that the increasing use of agreements with confidential rebates and discounts have had a negative impact on price transparency, potentially leading to outcomes that are inefficient or not conducive to good governance. High prices of cancer medicines may have inadvertently caused inefficient R&D practices as well as unethical or illegal business practices. Evidence presented in this chapter shows that without appropriate interventions patient access to cancer medicines and the long-term financial sustainability of health care systems would be compromised. Based on the evidence presented, the following chapter presents the options that might enhance the availability and affordability of cancer medicines, as suggested by the Informal Advisory Group.

5 Options that might enhance the affordability and accessibility of cancer medicines

This chapter presents a set of options that might enhance the affordability and accessibility of cancer medicines. These options should be applied in combination with a view to creating a holistic approach to achieving affordable prices for and access to medicines and optimal outcomes for patients, as per the goals of the national medicines policies (Section 3.1). Fig. 5.1 presents a diagrammatic summary of these options, which are described in detail in the next section.

Fig. 5.1: Summary of options that might enhance the affordability and accessibility of cancer medicines


Strengthening pricing policies at the national and regional levels
Improving efficiency of expenditure on cancer medicines
Improving transparency of pricing approaches and prices
Promoting collaboration cross-sector & cross-border information-sharing, regulation & procurement
Managing demand-side factors influencing medicines utilization
Realigning incentives for research and development

1 Improving the consistency of policies across health and other sectors
2 Designing differential pricing sensitive to health systems' ability to pay
3 Enhancing system ability to review and adjust prices, and withdraw funding for superseded or less cost-effective medicines if required
4 Enforcing price caps for cancer medicines, with or without progressive reduction of prices over time
5 Creating competition among substitutable cancer medicines, with respect to price, quality and ability to supply

1 Prioritizing the selection of medicines with high(er) clinical value
2 Considering the costs of model of care as part of pricing approach
3 Considering managed entry agreements for expenditure control only in specific cases
4 Avoiding the use or establishment of funds earmarked for the provision of cancer medicines

1 Disclosing the net transaction prices of cancer medicines to relevant stakeholders
2 Disclosing and controlling prices along the supply chain
3 Reporting the costs of research, development and production, including any public sources of funding
4 Communicating pricing and reimbursement decisions to the public when appropriate

1 Sharing information on medicine prices and technical assessments
2 Harmonizing regulatory requirements for biosimilar medicines to ensure safety and quality, and to promote competition
3 Streamlining cross-border regulatory requirements and supply management of medicines in shortage
4 Pooling subnational, national and regional resources for joint negotiation and procurement
5 Using voluntary license agreements where possible and applying WTO TRIPS flexibilities for patented medicines where appropriate

1 Removing financial/non-financial incentives for prescribing cancer medicines of limited clinical value
2 Restricting promotional activities of cancer medicines to clinicians and the public
3 Correcting any misperception of inferior quality of generic or biosimilar medicines
4 Implementing regulatory measures upon identification of substandard and falsified medicines

1 Incentivizing research for cancers affecting smaller populations
2 Focusing on health service research to improve system efficiencies, rational use of medicines and packages of care

5.1 Strengthening pricing policies at the national and regional levels

5.1.1 Improving the consistency of policies across health and other sectors

Rationale: Evidence suggests that inconsistent policies for managing medicine prices across health care services and the supply chain over time could result in uncontrolled and highly dispersed prices for the same medicine. These would not only result in ineffective control of medicine prices, but also potentially cause inefficient cost-shifting activities and inequitable patient access to treatment (Section 4.1.3). Consistent and holistic price regulations have been shown to have achieved lower prices (Section 4.1.4). In addition, pricing policies for medicines should seek alignment with policies in market competition, trade and industry development, with a view to seeking common goals to enhance efficiency and welfare (Sections 4.1.5 and 4.4.1).

Considerations: When setting a pricing policy, it is important to have a clear understanding of the problems, purposes and goals. Pricing policy should interact with the broader systems and processes (e.g. legal system), so that policy recommendations are implementable and would meet the needs of the systems and decision-makers. The overall policy framework should gain political supports from all relevant stakeholders so that policy implementation is purposeful and efficient.

5.1.2 Designing differential pricing sensitive to health systems' ability to pay

Rationale: Evidence shows that the prices of cancer medicines seem commensurate neither with demand, nor a country's purchasing power (Section 4.1.2), resulting in unaffordability of cancer medicines in lower-income countries (Section 4.3). Differential pricing is a pricing approach where prices are differentiated according to countries' characteristics, such as disease burden and wealth as measured by gross domestic product per capita. Differential pricing has been proposed (*397,398*) and applied to improve access to medicines (e.g. hepatitis C medicines (*399*)). However, country groupings based on gross national income per capita may not be sensitive to the health systems' actual ability to pay, particularly in middle-income countries.

Considerations: Differential pricing may reflect the health system design, existing health expenditure, population needs and ability to pay. Pricing would need to be transparent to assess fairness.

5.1.3 Enhancing system ability to review and adjust prices, and withdraw funding for superseded or less cost-effective medicines if required

Rationale: It is important to monitor and revise medicine prices according to changing market conditions or therapeutic landscape so that the prices would reflect the medicines' comparative value in the changing market (Section 3.3.2). When medicines have been superseded by newer or more cost-effective treatment, health systems may consider divestment from these products. Divestment would "reduce unwarranted variations in clinical practice and allow a re-allocation of resources from low-value to high-value services/programmes" (*400*). Pricing policies should set clear rules about price increases and pharmaceutical companies should be required to provide justifications for any price increase.

Considerations: Price adjustments may be applied along the value chain or at different time points of the product life-cycle (Fig. 1.3). Frequency of price revision should be sensitive to changing market conditions and therapeutic landscape, but it would need to be pragmatic in order to create reasonable stability in prices and avoid excessive administrative costs.

5.1.4 Considering the enforcement of price caps for cancer medicines, with or without progressive reduction of prices over time

Rationale: Price-cap regulation has been applied to bind market prices or to prevent the increase of medicine prices for a predetermined period of time without a justification (Section 0). Such regulation is particularly pertinent in contexts where existing regulations, or the lack thereof, have not sufficiently controlled price increases, leading to medicine prices that are unsustainable to the long-term robustness of the health care system (Sections 4.1.3). In contexts where current prices of cancer medicines clearly impede the ability of the health care system to delivery universal health coverage for cancer patients (Section 4.3), countries may consider implementing progressive reduction of prices over time, with a view to correcting unsustainable and unaffordable prices. From the system perspective, these initiatives may also encourage companies to seek greater efficiencies by reducing their costs in order to maintain or even improve their profit margins.

Considerations: Correction of unaffordable prices of cancer medicines would require considerable short-term system adjustments. It would also require strong political commitment as well as stakeholder engagement. Operationally, it would require setting clear rules about the implementation of price reduction (e.g. frequency and magnitude) and circumstances where rules might be exempted. Authorities would also need to have the necessary authority and resources to enforce the implementation.

5.1.5 Creating competition among substitutable cancer medicines, with respect to price, quality and ability to supply

Rationale: Price and market competition among manufacturers of clinically substitutable medicines (i.e. me-too medicines, generic and biosimilar products) has led to lower prices and generates expenditure savings (Section 4.1.5). Pricing and procurement policies should encourage competition on criteria and contract terms other than price (e.g. ability to supply, product quality) and take a long-term view on shaping a competitive environment. This would avoid creating an oligopolistic market with a small number of suppliers, where the suppliers may exercise their market power to dictate the price, or compromise the continuity of supply or the quality of the product supplied (Sections 3.3.1.4 and 4.6.2).

Considerations: The policy would need to ensure that any price reduction and savings are transferred to consumers or governments. For this reason, pricing policy would need to work in conjunction with the enforcement of robust competition policies and good governance in order to reap the full benefits of competition, as well as to prevent anti-competitive behaviours and other business practices that may impair system efficiency (Section 4.1.5)

5.2 Improving the efficiency of expenditure on cancer medicines

5.2.1 Prioritizing the selection of medicines with high(er) clinical value

Rationale: Judicious selection of cancer medicines and rational application of access requirements with consideration to specific health system context can deliver better value for money for patients and the health care system, particularly for newer high-cost medicines of low clinical value (Chapter 2 and Section 4.2.3).

Considerations: A policy of funding additional new cancer medicines in order to achieve numerical parity with other countries would not result in substantive health improvement and would significantly increase costs. Countries should enhance the capacity of their systems to provide cancer medicines, as well as other modalities of cancer care, in line with their populations' epidemiological profiles.

5.2.2 Considering the costs of model of care as part of pricing approach

Rationale: Pricing of cancer medicines must account for the costs of other associated clinical and non-clinical services. These include the use of laboratory tests to determine the cancer genetic profile in order to guide treatment selection; preparation, delivery and administration of the medicines; as well as treatments to prevent myelosuppression.

Considerations: A thorough assessment of the clinical profile of medicines and mapping of the clinical service pathway would help to inform major cost components associated with the use of cancer medicines. A full health technology assessment or micro-costing study e.g. (*401*) may be helpful, but not essential.

5.2.3 Considering managed entry agreements for expenditure control only in specific cases

Rationale: MEAs may be used in anticipation of high expenditure or when the medicines present evidence with uncertain benefits or harms at the time of decision-making. However, the use of these agreements should only be in highly selective circumstances, where there is a clear clinical need for the medicine, and access would be jeopardized in the absence of the agreement (Section 0). These agreements should avoid confidential terms, as they would reduce market transparency and good governance (Section 4.5).

Considerations: MEAs may be associated with high transaction and administrative costs. The agreements may not address clinical uncertainties unless a robust data collection and scientific approach are in place (Section 4.5), which in turn, would add to the overall costs of implementing such policy.

5.2.4 Avoiding the use or establishment of funds earmarked for the provision of cancer medicines

Rationale: Society does not always consistently support a preference for health gains in cancer compared to other health conditions. The use of earmarked funds for the provision of cancer medicines would create unfair access to medicines used for other diseases as it may divert limited resources away from use in other diseases. Past experience of using funds earmarked for the provision of cancer medicines has increased costs, failed to deliver meaningful benefits to patients and society and not expedited access to medicines (Section 4.1.5).

Considerations: The use of small-scale and limited earmarked funds may be justifiable for medicines with established clinical and safe profiles if access to these medicines would not be possible in the absence of such a fund. NGOs and patient groups often aim to serve limited if not single interest (e.g. only for people with certain cancer). Governments should engage and inform these organizations about the shortcomings of earmarked funds.

5.3 Improving the transparency of pricing approaches and prices of cancer medicines

5.3.1 Disclosing the net transaction prices of cancer medicines to relevant stakeholders

Rationale: The use of discounts and rebates may signal competition in the market and is often considered a legitimate competitive practice if applied within the boundaries of laws. However, use of confidential rebates and discounts have reduced market transparency and the practice is not consistent with good governance

(Section 4.5.2). The growing gaps between list price and net transaction price might invite a perception that the industry has been pushing medicine prices higher by factoring in a higher level of discounts, with a view to masking the true price increases at the level of individual medicines (Section 4.5.2).

Considerations: The impacts of transparency in medicine prices are not clear and remain theoretical. Medicine prices and market dynamics after the implementation of a transparency initiative should be monitored.

5.3.2 Disclosing and controlling prices along the supply chain

Rationale: Authorities in some countries have implemented regulations on mark-ups along the supply and distribution chains to control medicine prices (Section 0). Clear rules and regulations would assist with enhancing the transparency, monitoring and control of medicine prices and ensuring affordability to patients.

Considerations: The effectiveness of this measure is dependent on the regulators' visibility of the supply and distribution chains, as well as the capacity and ability to enforce non-compliance. The design of the rules and regulations should be straightforward and implementable.

5.3.3 Reporting the costs of research, development and production, including any public sources of funding

Rationale: The costs of R&D have been used to justify the prices of cancer medicines: return on investment needs to be sufficient to cover the costs of past R&D and to incentivize the discovery of future medicines. However, there is considerable paucity of data on the costs of R&D and production because of the proprietary nature of the information (Section3.2). Furthermore, the public sector has provided significant contributions towards drug discovery through direct funding or R&D incentives (Section 4.4.2). In any case, the costs of R&D and production may bear little or no relationship to how pharmaceutical companies set prices of cancer medicines (Section 3.2.1.5). Reporting the costs of R&D and production, including any public sources of funding, would inform the debate on medicine pricing as well as how to manage the relationship between the government, industry and university when pursuing joint research ventures.

Considerations: Any policy to mandate reporting should consider the global nature of R&D and production. Attribution of public funding for basic science research and research not specific to an anatomical site would be challenging and would require careful planning.

5.3.4 Communicating pricing and reimbursement decisions to the public when appropriate

Rationale: When appropriate, the public should be informed about the rationale underlying pricing and reimbursement decisions. This would help to foster a common understanding among affected stakeholders and promote accountability. It would also help to avoid unnecessary lobbying activities, which is wasteful and may distort the fairness of resource allocation.

Considerations: The public or relevant stakeholders should also be informed about the purpose of involvement and how their inputs might inform decision-making. The public and relevant stakeholders should be consulted regarding the method of communication (*402*).

5.4 Promoting cross-sector & cross-border collaboration for information-sharing, regulation & procurement

5.4.1 Sharing information on medicine prices and technical assessments

Rationale: Sharing of pricing information may assist with improving transparency of prices. Implementing health technology assessment to determine value and price of medicines requires resources and strong capability for performing appraisals and technical analyses. These elements are not always available, particularly in low- and middle-income countries, resulting in assessments of variable comprehensiveness and robustness. Sharing of information on technical assessments would therefore avoid duplication of effort and might foster collaboration (Section 3.3.1.2).

Considerations: Countries or settings would still need to build capacity for interpreting the shared information before generalizing the findings to their respective contexts.

5.4.2 Harmonizing regulatory requirements for biosimilar medicines to ensure safety and quality, and to promote competition

Rationale: Application of intellectual property rights keeps generic or biosimilar competition out of the market for varying periods of time depending on the jurisdiction. Many cancer medicines have generated substantial financial returns for the originator companies after loss of market exclusivity, particularly for biologics (Section 3.2.1.5). Furthermore, originator companies may initiate patent disputes to discourage or delay market entry of generic or biosimilar medicines (Section 3.2.2.2). Despite efforts towards international harmonization of regulatory requirements for biosimilar products, varying rules regarding nomenclature and substitution in some jurisdictions may have created barriers for the introduction of these products, indirectly reducing the level of price and market competition.

Considerations: Harmonizing regulatory requirements for biosimilar medicines would require cross-border collaboration and political commitments. As one of the steps to improve capacity to assess and approve products more rapidly and with greater efficiency, WHO has implemented pilot prequalification of biosimilar products for rituximab and trastuzumab in 2018 (*403*).

5.4.3 Streamlining cross-border regulatory requirements and supply management of medicines in shortage

Rationale: In recent years, the supplies of some cancer medicines have been disrupted, causing shortages. However, the frequency of shortages seems to be decreasing (Section 4.6.2). Notwithstanding, in the event of shortage, streamlining cross-border supply of medicines with appropriate oversights would ensure continuity of supply.

Considerations: Political commitments and alignment of legal, regulatory and policy requirements are essential.

5.4.4 Pooling subnational, national and regional resources for joint negotiation and procurement

Rationale: Pooled procurement has been used at the subnational, national or regional levels in various jurisdictions to create greater purchasing power through economies of scale, as well as greater efficiency through sharing of human resources (i.e. expertise and workload) and possible streamlining of procurement processes (Section 3.3.3.2).

Considerations: The success of pooled procurement requires a number of facilitating factors particularly when the arrangement involves multiple jurisdictions, including political commitment, alignment of legal, regulatory and policy requirements and processes, and ability to address local needs (Section 3.3.3.2).

5.4.5 Using voluntary license agreements where possible and applying WTO TRIPS flexibilities for patented medicines where appropriate

Rationale: Cancer medicines under the protection of intellectual property are unaffordable to patients and health care systems in low- and middle-income countries. Countries may negotiate price and volume agreements with manufacturers that hold the intellectual property. If this fails, countries may seek voluntary license agreements through negotiation with the patent holders to enable procurement of generic or biosimilar medicines. If both price-volume negotiation and the use of voluntary license agreement do not lead to affordable prices, countries may consider using the World Trade Organization (WTO) Trade-Related Aspects of Intellectual Property Rights (TRIPS) flexibilities for patented medicines where appropriate.

Considerations: Prior to seeking a voluntary license agreement, the patent and data exclusivity status of the specific cancer medicines in a particular jurisdiction(s) should be clarified. Such agreement should be sought preferably across jurisdictions where there is a common need for the medicine (e.g. disease burden). Countries should also clarify the capacity and willingness of alternative manufacturer(s) to produce the generic/biosimilar cancer medicines. Where required, in particular for low- and middle-income countries, countries may seek support from the Medicines Patent Pool to facilitate the negotiation of voluntary license agreement. In general, voluntary license agreements should be non-restrictive, that is, with terms and conditions that encompass wide geographical scope, non-exclusive licenses to encourage competition, including waivers for data exclusivity, and compatible with the use of TRIPS flexibilities (e.g. compulsory licenses).

5.5 Managing factors that would influence demand for medicines

5.5.1 Removing financial/non-financial incentives for prescribing cancer medicines of limited clinical value

Rationale: Health care professionals are de facto agents for patients and health care systems; they may however not be acting in the best interest of either, especially when there are financial or non-financial incentives for prescribing certain medicines. This is because health care professionals who prescribe or dispense the medicine do not pay for the medicine, while patients or health systems pay for the medicine but do not choose it. Removing perverse incentives would strengthen the "agency relationship" and enhance system efficiency by lowering the utilization of cancer medicines of limited clinical value, to which pharmaceutical companies are more likely to apply additional incentives to induce prescribing through promotional activities (*404*).

Considerations: Requiring health care professionals to disclose any potential conflict of interest due to relationship with the pharmaceutical industry, perceived or actual, is an important first step for removing financial and non-financial incentives for prescribing cancer medicines of limited clinical value. The enforcement of disclosure would require strong commitments (e.g. (*405*)), effective stakeholder engagements to foster a common understanding, as well as having standardized reporting processes to ensure that disclosure is not burdensome.

5.5.2 Restricting promotional activities of cancer medicines to clinicians and the public

Rationale: A significant proportion of the expenditure reported by pharmaceutical companies is for marketing and promotional activities (Section 3.2.1.2). While marketing and promotional activities may enhance information sharing, it is important to recognize that the primary aim of these activities is to influence the utilization of medicines. In some cases, it may lead to unethical business practices (Section 4.1.5). Reducing the costs of marketing might translate into a reduction in the costs, and by extension prices of medicine.

Considerations: Restricting non-price competition through promotional activities may have an indirect effect of encouraging price competition.

5.5.3 Correcting any misperception of inferior quality of generic or biosimilar medicines

Rationale: Low uptake of generic and biosimilar medicines due to misperception of inferior quality of these medicines may impair price competition. Furthermore, originator and their contracting companies may refer their marketed generic medicines as "branded generics" or "quality generics" to seek differentiation from other genuinely generic medicines, despite the latter having equally met the necessary regulatory requirements for quality.

Considerations: When necessary and appropriate, authorities may implement policies to mandate the prescribing or dispensing of generic or biosimilar products (Table 3.6).

5.5.4 Implementing regulatory measures upon identification of substandard and falsified medicines

Rationale: There have been reported cases of substandard and falsified cancer medicines (Section 4.6.3). The emergence of these products may cause harm to patients because of their inferior quality or due to failure to treat the disease. Substandard and falsified generic and biosimilar medicines would also reduce public confidence in using these medicines, thereby impairing price competition. The emergence of counterfeit medicines is primarily motivated by profit making. It could also be due to patients having to resort to unauthorized channels so that they could gain access to affordable medicines.

Considerations: The regulator would need to have the capacity and ability to undertake surveillance to detect substandard and falsified medicines. Upon detection, the regulators would need to inform health care practitioners rapidly, as well as launch legal prosecution to deter future criminal activities.

5.6 Realignment of incentives for research and development

5.6.1 Incentivizing research for cancers affecting smaller populations

Rationale: Despite the challenges in identifying financing gaps for R&D on cancer medicines because of technical complexity and value judgment (see Section 4.4.3), there seems to be a common understanding that there is an unmet need for R&D for cancers affecting smaller populations, such as paediatric and young adult cancer populations, and adults with rare cancers. The lack of R&D for medicines for use in these populations have led to widespread off-label use of medicines and potential inequitable access to medicines because of non-standardized guidance.

Considerations: The US FDA and the European Medicines Agency have implemented regulatory initiatives to enable and stimulate research into the uses of medicines in children and young people (*406*,*407*). These include development of priority lists of off-patent medicinal products for which studies are required and establishing review committees specialized in paediatric medicines. As outlined in Section 4.6.1.1, there is a range of policy incentives to stimulate the R&D of medicines for rare diseases, including rare cancers. However, as noted, the incentives need to be realigned in order to avoid the potential consequence of unintendedly leading companies to pursue an orphan indication in the first instance then expand to other non-rare indications, with a view to gaining faster market entry at high prices.

5.6.2 Focusing on health service research to improve system efficiencies, rational use of medicines and packages of care

Rationale: Many problems and challenges related to the provision of cancer medicines are likely to be common across other parts of the health care system. There is evidence that access to adequate cancer care other than access to cancer medicines remains inequitably distributed between and within countries. Governments should continue to focus on implementing a spectrum of interventions to mitigate the current and future impacts of cancer, ranging from prevention of risk factors to palliation of people with cancer (Section 1.1). Health service research may identify the key barriers of access to existing therapies, the removal of which would encourage better patient access.

Furthermore, incentives may be given to research that focuses on clarifying rational and high-quality use of medicines. These include the duration of treatment. For example, a recent study found that the use of trastuzumab in the adjuvant setting for women with HER2-positive breast cancer for 9 weeks resulted in shorter disease-free survival than the standard 1-year regimen, but the shorter treatment was associated with fewer cardiac adverse effects and better maintained cardiac function (*408*). Research such as this helps clinicians to weigh the risks of benefits of having longer or shorter courses of therapy.

Considerations: Health service research must seek to inform delivery of services and be relevant to decision-makers. Researchers must be cognizant of the potential sensitive nature of health service research (e.g. that it may identify inefficient practices) and seek to manage any potential restrictions on public release of research findings (*409*).

5.7 Conclusion

While some of the evidence presented in this report has limitations, the totality of evidence suggests that current pricing policy for cancer medicines has not adequately met health- and economic-related objectives. Prices of medicines are high in both absolute and relative terms compared to other therapeutic areas. Some stakeholders have influenced medicine prices higher than the true clinical value of cancer medicines, essentially lending higher negotiation power to the pharmaceutical industry. This power imbalance compromises the ability of the system and individuals to pay for these medicines, and deliver quantities less than what would be required for maximizing societal welfare.

The enduring debates on unaffordability of cancer medicines and the ever-growing list of medicines and combination therapies with annual costs in the hundreds of thousands suggest that the status quo is not acceptable. The global community must come together to find a way to correct the irrational behaviours that have led to unsustainable prices of cancer medicines. As these behaviours are not exclusive to cancer medicines, mitigation strategies must include price control over other medicines, health products and health services more generally. Global correction of unaffordable prices of cancer medicines will require considerable short-term system adjustments, but such adjustments are fundamental to the sustainability of access to cancer medicines, and medicines in general in the long term. The R&D system will also require re-alignment of incentives so that limited resources are directed towards activities that will deliver true innovation and value to patients efficiently. Further inertia on this issue and half-hearted commitments from all stakeholders to address the problems, including governments and the pharmaceutical industry, will only invite distrust and disengagement from the public.

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Appendices

Appendix A: Resolution WHA70.12

Appendix B: Five-year age standardized survival rates for cancers

Appendix C: Members of informal advisory groups

Appendix D: List of key publications relating to reviews of medicine pricing

Appendix E: Health expenditure on pharmaceuticals and disease burden

Appendix A: Resolution WHA70.12

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Cancer prevention and control in the context of an integrated approach

The Seventieth World Health Assembly,

Having considered the report on cancer prevention and control in the context of an integrated approach[xxiii];

Acknowledging that, in 2012, cancer was the second leading cause of death in the world with 8.2 million cancer-related deaths, the majority of which occurred in low-and middle-income countries;

Recognizing that cancer is a leading cause of morbidity globally and a growing public health concern, with the annual number of new cancer cases projected to increase from 14.1 million in 2012 to 21.6 million by 2030;

Aware that certain population groups experience inequalities in risk factor exposure and in access to screening, early diagnosis and timely and appropriate treatment, and that they also experience poorer outcomes for cancer; and recognizing that different cancer control strategies are required for specific groups of cancer patients, such as children and adolescents;

Noting that risk reduction has the potential to prevent around half of all cancers;

Aware that early diagnosis and prompt and appropriate treatment, including pain relief and palliative care, can reduce mortality and improve the outcomes and quality of life of cancer patients;

Recognizing with appreciation the introduction of new pharmaceutical products based on investment in innovation for cancer treatment in recent years, and noting with great concern the increasing cost to health systems and patients;

Emphasizing the importance of addressing barriers in access to safe, quality, effective and affordable medicines, medical products and appropriate technology for cancer prevention, detection, screening diagnosis and treatment, including surgery, by strengthening national health systems and international cooperation, including human resources, with the ultimate aim of enhancing access for patients, including through increasing the capacity of the health systems to provide such access;

Recalling resolution WHA58.22 (2005) on cancer prevention and control;

Recalling also United Nations General Assembly resolution 66/2 (2011) on the Political Declaration of the High-level Meeting of the General Assembly on the Prevention and Control of Non-Communicable Diseases, which includes a road map of national commitments from Heads of State and Government to address cancer and other noncommunicable diseases;

Recalling further resolution WHA66.10 (2013) endorsing the global action plan for the prevention and control of noncommunicable diseases 2013–2020, which provides guidance on how Member States can realize the commitments they made in the Political Declaration of the High-level Meeting of the General Assembly on the Prevention and Control of Non-communicable Diseases, including those related to addressing cancer;

[xxiii] Document A70/32.

Recalling in addition United Nations General Assembly resolution 68/300 (2014) on the Outcome document of the high-level meeting of the General Assembly on the comprehensive review and assessment of the progress achieved in the prevention and control of non-communicable diseases, which sets out the continued and increased commitments that are essential in order to realize the road map of commitments to address cancer and other noncommunicable diseases included in the Political Declaration of the High-level Meeting of the General Assembly on the Prevention and Control of Non-communicable Diseases, including four time-bound national commitments for 2015 and 2016;

Mindful of the existing monitoring tool that WHO is using to track the extent to which its 194 Member States are implementing these four time-bound commitments to address cancer and other noncommunicable diseases, in accordance with the technical note published by WHO on 1 May 2015 pursuant to decision EB136(13) (2015);

Mindful also of the WHO Framework Convention on Tobacco Control;

Also mindful of the Sustainable Development Goals of the 2030 Agenda for Sustainable Development, specifically Goal 3 (Ensure healthy lives and promote well-being for all at all ages) with its target 3.4 to reduce, by 2030, premature mortality from noncommunicable diseases by one third, and target 3.8 on achieving universal health coverage;

Appreciating the efforts made by Member States and international partners in recent years to prevent and control cancer, but mindful of the need for further action;

Reaffirming the global strategy and plan of action on public health, innovation and intellectual property;

Reaffirming also the rights of Member States to the full use of the flexibilities in the WTO Agreement on Trade-related Aspects of the Intellectual Property Rights (TRIPS) to increase access to affordable, safe, effective and quality medicines, noting that, inter alia, intellectual property rights are an important incentive in the development of new health products,

1. URGES Member States, taking into account their context and institutional and legal frameworks, as well as national priorities:

   (1) to continue to implement the road map of national commitments for the prevention and control of cancer and other noncommunicable diseases included in United Nations General Assembly resolutions 66/2 (2011) on the Political Declaration of the High-level Meeting of the General Assembly on the Prevention and Control of Non-communicable Diseases and 68/300 (2014) on the Outcome document of the high-level meeting of the General Assembly on the comprehensive review and assessment of the progress achieved in the prevention and control of non-communicable diseases;

   (2) to also implement the four time-bound national commitments for 2015 and 2016 set out in the Outcome document, in preparation for a third High-level Meeting of the General Assembly on the Prevention and Control of Non-communicable Diseases, to be held in 2018, taking into account the technical note published by WHO on 1 May 2015, which sets out the progress indicators that the Director-General will use to report to the United Nations General Assembly in 2017 on the progress achieved in the implementation of national commitments, including those related to addressing cancer, taking into account cancer-specific risk factors;

(3) to integrate and scale up national cancer prevention and control as part of national responses to noncommunicable diseases, in line with the 2030 Agenda for Sustainable Development;

(4) to develop, as appropriate, and implement national cancer control plans that are inclusive of all age groups; that have adequate resources, monitoring and accountability; and that seek synergies and cost-efficiencies with other health interventions;

(5) to collect high-quality population-based incidence and mortality data on cancer, for all age groups by cancer type, including measurements of inequalities, through population-based cancer registries, household surveys and other health information systems in order to guide policies and plans;

(6) to accelerate the implementation by States Parties of the WHO Framework Convention on Tobacco Control; and, for those Member States that have not yet done so, to consider acceding to the Convention at the earliest opportunity, given that the substantial reduction of tobacco use is an important contribution to the prevention and control of cancer; and to act to prevent the tobacco industry's interference in public health policy for the success of reducing the risk factors of noncommunicable diseases;

(7) to promote the primary prevention of cancers;

(8) to promote increased access to cost-effective vaccinations to prevent infections associated with cancers, as part of national immunization schedules, based on country epidemiological profiles and health systems' capacities, and in line with the immunization targets of the global vaccine action plan;

(9) to develop, implement and monitor programmes, based on national epidemiological profiles, for the early diagnosis of common cancers, and for screening of cancers, according to assessed feasibility and cost-effectiveness of screening, and with adequate capacity to avoid delays in diagnosis and treatment;

(10) to develop and implement evidence-based protocols for cancer management, in children and adults, including palliative care;

(11) to collaborate by strengthening, where appropriate, regional and sub-regional partnerships and networks in order to create centres of excellence for the management of certain cancers;

(12) to promote recommendations that support clinical decision-making and referral based on the effective, safe and cost-effective use of cancer diagnostic and therapeutic services, such as cancer surgery, radiation and chemotherapy; and to facilitate cross-sectoral cooperation between health professionals, as well as the training of personnel at all levels of health systems;

(13) to mobilize sustainable domestic human and financial resources and consider voluntary and innovative financing approaches to support cancer control in order to promote equitable and affordable access to cancer care;

(14) to promote cancer research to improve the evidence base for cancer prevention and control, including research on health outcomes, quality of life and cost-effectiveness;

(15) to provide pain relief and palliative care in line with resolution WHA67.19 (2014) on the strengthening of palliative care as a component of comprehensive care throughout the life course;

(16) to anticipate and promote cancer survivor follow-up, late effect management and tertiary prevention, with the active involvement of survivors and their relatives;

(17) to promote early detection of patients' needs and access to rehabilitation, including in relation to work, psychosocial and palliative care services;

(18) to promote and facilitate psychosocial counselling and aftercare for cancer patients and their families, taking into account the increasingly chronic nature of cancer;

(19) to continue fostering partnerships between government and civil society, building on the contribution of health-related nongovernmental organizations and patient organizations, to support, as appropriate, the provision of services for the prevention and control, treatment and care of cancer, including palliative care;

(20) to work towards the attainment of Sustainable Development Goal 3, target 3.4, reiterating the commitment to reduce, by 2030, premature mortality from cancer and other non-communicable diseases by one third;

(21) to promote the availability and affordability of quality, safe and effective medicines (in particular, but not limited to, those on the WHO Model List of Essential Medicines), vaccines and diagnostics for cancer;

(22) to promote access to comprehensive and cost-effective prevention, treatment and care for the integrated management of cancers including, inter alia, increased access to affordable, safe, effective and quality medicines and diagnostics and other technologies;

2. REQUESTS the Director-General:

(1) to develop or adapt stepwise and resource-stratified guidance and tool kits in order to establish and implement comprehensive cancer prevention and control programmes, including for the management of cancers in children and adolescents, leveraging the work of other organizations;

(2) to collect, synthesize and disseminate evidence on the most cost-effective interventions for all age groups, and support Member States in the implementation of these interventions; and to make an investment case for cancer prevention and control;

(3) to strengthen the capacity of the Secretariat both to support the implementation of cost-effective interventions and country-adapted models of care and to work with international partners, including IAEA, to harmonize the technical assistance provided to countries for cancer prevention and control;

(4) to work with Member States, and collaborate with nongovernmental organizations, private sector entities, philanthropic foundations and academic institutions as defined in the Framework of Engagement with Non-State Actors in order to develop partnerships to scale up cancer prevention and control, and to improve the quality of life of cancer patients, in line with Sustainable Development Goals 3 (Ensure healthy lives and promote well-being for all at all ages) and 17 (Strengthen the means of implementation and revitalize the global partnership for sustainable development);

(5) to strengthen the collaboration with nongovernmental organizations, private sector entities, academic institutions and philanthropic foundations, as defined in WHO's Framework for Engagement with Non-State Actors, with a view to fostering the development of effective and affordable new cancer medicines;

(6) to provide technical assistance, upon request, to regional and subregional partnerships and networks, including, where appropriate, support for the establishment of centres of excellence to strengthen cancer management;

(7) to develop, before the end of 2019, the first periodic public health-and policy-oriented world report on cancer, in the context of an integrated approach, based on the latest available evidence and international experience, and covering the elements of this resolution, with the participation of all relevant parts of WHO, including IARC, and in collaboration with all other relevant stakeholders, including cancer survivors;

(8) to enhance the coordination between IARC and other parts of WHO on assessments of hazards and risks, and on the communication of those assessments;

(9) to prepare a comprehensive technical report to the Executive Board at its 144th session that examines pricing approaches, including transparency, and their impact on availability and affordability of medicines for the prevention and treatment of cancer, including any evidence of the benefits or unintended negative consequences, as well as incentives for investment in research and development on cancer and innovation of these measures, as well as the relationship between inputs throughout the value chain and price setting, financing gaps for research and development on cancer, and options that might enhance the affordability and accessibility of these medicines;

(10) to synchronize the periodic report on progress made in implementing this resolution with, and integrate it into, the monitoring and report timeline of the prevention and control of non-communicable diseases, set out in resolution WHA66.10.

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Appendix B: Five-year age standardized survival rates for cancers

Source: CONCORD Working Group, Allemani C, Matsuda T, Di Carlo V, Harewood R, Matz M, et al. Global surveillance of trends in cancer survival 2000–14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. Lancet. 2018;14 (http://linkinghub.elsevier.com/retrieve/pii/S0140673617333263, accessed 13 November 2018).

Site	Absolute percentage increase in survival rate 2000–2004 and 2010–2014	Survival rate 2010–2014
Oesophagus	**+12.7%**: Republic of Korea **+6–10%**: Puerto Rico, China, Israel, Japan, Singapore, Ireland, Norway, Portugal, Belgium, the Netherlands, Switzerland, Australia **+4–5%**: Denmark, the United Kingdom, Germany, USA	**>30%**: Japan, Republic of Korea **20–30%**: Puerto Rico, USA, China, Israel, Ireland, Belgium, Germany, the Netherlands, Switzerland, Australia
Stomach	**+>20%**: China, Republic of Korea **+6–10%**: Canada, Israel, Japan, Estonia, Ireland **+11%**: USA, Germany **+5%**: Denmark, Lithuania, the United Kingdom, Poland, Austria, the Netherlands	**60–70%**: Republic of Korea, Japan **30–40%**: Canada, USA, Puerto Rico, Martinique, Malaysia, Singapore, China, Taiwan (China), Israel, Italy, Portugal, Austria, Belgium, Germany, Switzerland, Australia **20–29%**: Mauritius, Kuwait, Turkey, 20 European countries, New Zealand **<20%**: Chile, Ecuador, India, Thailand, Bulgaria
Colon	**+10%**: China, Israel, Republic of Korea, Denmark, Iceland, Latvia, Norway, the United Kingdom, Portugal, Slovenia, Spain, Bulgaria, Czech Republic, Poland, Germany, Switzerland **+5–10%**: Canada, Japan, Taiwan (China), Estonia, Finland, Ireland, Lithuania, Sweden, Italy, Malta, Austria, France, the Netherlands, Australia	**>70%**: Israel, Republic of Korea, Australia **60–69%**: Costa Rica, Puerto Rico, Canada, USA, Japan, Singapore, Taiwan (China), Denmark, Finland, Iceland, Ireland, Norway, Sweden, the United Kingdom, Italy, Portugal, Slovenia, Spain, Austria, Belgium, France, Germany, the Netherlands, Switzerland, New Zealand **50–60%**: Mauritius, Martinique, Peru, Uruguay, Malaysia, China, Hong Kong Special Administrative Region (SAR), Kuwait, Turkey, Estonia, Lithuania, Latvia, Croatia, Malta, Bulgaria, Czech Republic, Poland, Slovakia **<50%**: Ecuador, Thailand, Russian Federation, India
Rectum	**+>20%**: China, Republic of Korea, Slovenia **+10–20%**: Canada, Israel, Republic of Korea, Denmark, Estonia, Iceland, Ireland, Latvia, Lithuania, Norway, the United Kingdom, Portugal, Spain, Bulgaria, Czech Republic, Poland, Germany, the Netherlands, Switzerland, Australia **+5–10%**: Japan, Taiwan (China), Turkey, Austria, Finland, France, Italy, Malta, Sweden, New Zealand	**>70%**: Republic of Korea, Australia **60–69%**: Canada, USA, Singapore, Japan, Taiwan (China), Israel, Denmark, Finland, Iceland, Ireland, Norway, Sweden, the United Kingdom, Italy, Portugal, Slovenia, Spain, Austria, Belgium, France, Germany, the Netherlands, Switzerland, New Zealand **50–59%**: Argentina, Costa Rica, Martinique, Peru, Puerto Rico, Uruguay, Malaysia, China, Hong Kong SAR, Kuwait, Turkey, Estonia, Latvia, Lithuania, Malta, Czech Republic, Romania **<50%**: Slovakia, Poland, Croatia, Bulgaria, Ecuador, Thailand, Russian Federation, India

Site	Absolute percentage increase in survival rate 2000–2004 and 2010–2014	Survival rate 2010–2014
Liver	**+5–10%**: Canada, USA, Japan, Denmark, Ireland, the United Kingdom, Italy, Spain, France, the Netherlands, Switzerland, Australia, New Zealand **+>10%**: China, Taiwan (China), Republic of Korea, Norway, Portugal, Sweden	**20–29%**: Republic of Korea, Singapore, Taiwan (China), Belgium, Italy **10–19%**: Canada, USA, Martinique, China, Kuwait, Turkey, Iceland, Ireland, Latvia, Norway, Sweden, the United Kingdom, Portugal, Spain, Poland, France, Germany, the Netherlands, Switzerland, Australia, New Zealand **<10%**: Denmark, Slovenia, Thailand, Czech Republic, Russian Federation, Estonia
Pancreas	**+3–5%**: Canada, USA, Republic of Korea, Singapore, Denmark, Estonia, Ireland, Latvia, Norway, Sweden, the United Kingdom, Portugal, Czech Republic, Belgium, the Netherlands, Switzerland, Australia	**>15%**: Kuwait (23.6%), Malaysia (Penang, 19.0%) **10–15%**: Canada, USA, Martinique, China, Republic of Korea, Turkey, Estonia, Ireland, Latvia, Norway, Sweden, Portugal, Belgium, Germany, Australia **4–9%**: 15 countries
Lung	**+>10%**: China, Republic of Korea **+5–10%**: Canada, USA, Israel, Japan, Taiwan (China), Denmark, Estonia, Iceland, Ireland, Latvia, Norway, Sweden, the United Kingdom, Portugal, Slovenia, Austria, France, Germany, the Netherlands, Switzerland, Australia	**20–33%**: Japan, Mauritius, Canada, USA, China, Taiwan (China), Republic of Korea, Israel, Latvia, Iceland, Sweden, Austria, Switzerland **10–19%**: Martinique, Puerto Rico, Malaysia, Singapore, Cyprus, Kuwait, Turkey, Denmark, Estonia, Finland, Ireland, Lithuania, Norway, the United Kingdom, Croatia, Italy, Malta, Portugal, Slovenia, Spain, Czech Republic, Poland, Russian Federation, Slovakia, Belgium, France, Germany, the Netherlands, Australia, New Zealand **<10%**: Thailand, Brazil, Bulgaria, India
Melanoma (skin)	**+5–10%**: Republic of Korea, Denmark, Estonia, Latvia, Lithuania, the United Kingdom, Croatia, Portugal, Slovenia, Bulgaria, Czech Republic, Poland, Belgium	**>90%**: USA, Denmark, Sweden, the United Kingdom, Belgium, France, Germany, the Netherlands, Switzerland, Australia, New Zealand **80–89%**: Canada, Israel, Estonia, Finland, Iceland, Ireland, Norway, Italy, Malta, Portugal, Slovenia, Spain, Czech Republic, Austria **70–79%**: Argentina, Brazil, Costa Rica, Puerto Rico, Latvia, Lithuania, Croatia, Poland, Romania, Slovakia **60–69%**: Singapore, Republic of Korea, Japan, Turkey, Bulgaria, Russian Federation **<60%**: Ecuador, China, Taiwan (China)
Breast	Not reported	**>85%**: Costa Rica, Martinique, Canada, USA, Israel, Japan, Republic of Korea, Denmark, Finland, Iceland, Norway, Sweden, the United Kingdom, Austria, Belgium, France, Germany, the Netherlands, Switzerland, Italy, Malta, Portugal, Spain, Australia, New Zealand **80–84%**: Argentina, Peru, Puerto Rico, Singapore, China, Hong Kong SAR, Taiwan (China), Turkey, Ireland, Czech Republic, Latvia, Slovenia **70–79%**: Cuba, Ecuador, Kuwait, Mongolia, Estonia, Lithuania, Croatia, Bulgaria, Poland, Romania, Russian Federation, Slovakia

Site	Absolute percentage increase in survival rate 2000–2004 and 2010–2014	Survival rate 2010–2014
Cervix	**+14.3%**: China **+8–10%**: India, Bulgaria, Estonia, Switzerland **+4–7%**: Cuba, Israel, Japan, Republic of Korea, Denmark, Ireland, Lithuania, Norway, the United Kingdom, Poland	**60–69%**: Canada, USA, Brazil, Puerto Rico, China, Hong Kong SAR, Singapore, Israel, Turkey, 18 countries in Europe, Australia, New Zealand **50–59%**: Argentina, Ecuador, Martinique, Peru, Uruguay, India, Kuwait, Latvia, Lithuania, Bulgaria, Poland, Russian Federation, Malta
Ovary	**+20%**: Japan **+10–20%**: Estonia, Latvia **+5–10%**: USA, Israel, Republic of Korea, Taiwan (China), Denmark, Iceland, Ireland, Norway, Sweden, Portugal, Spain, Bulgaria, Poland, France, Switzerland, Australia	**40–49%**: Canada, USA, Singapore, China, Taiwan (China), Republic of Korea, Japan, Israel, Turkey, Denmark, Estonia, Finland, Iceland, Latvia, Norway, Sweden, Portugal, Spain, Austria, Belgium, France, Germany, Switzerland, Australia **30–39%**: Argentina, Brazil, Ecuador, Puerto Rico, Kuwait, Thailand, Ireland, Lithuania, the United Kingdom, Croatia, Italy, Slovenia, Bulgaria, Czech Republic, Poland, Russian Federation, Slovakia, the Netherlands, New Zealand **<30%**: Malta, India
Prostate	**+>20%**: Japan, Republic of Korea, Malaysia, Denmark, Estonia, Ireland, Latvia, Lithuania, the United Kingdom, Slovenia, Bulgaria, Czech Republic, Poland **+10–20%**: Israel, Taiwan (China), Thailand, Finland, Iceland, Norway, Sweden, Croatia, Italy, Malta, Spain, France, Germany, the Netherlands, Switzerland, Australia **+5–10%**: Brazil, Ecuador, Canada, China, Turkey, Austria, Portugal, New Zealand	≈**100%**: Puerto Rico, Martinique, USA **90–100%**: Brazil, Costa Rica, Canada, Israel, Japan, Republic of Korea, Iceland, Ireland, Finland, Latvia, Lithuania, Norway, Sweden, Italy, Portugal, Spain, Austria, Belgium, France, Germany, Australia, New Zealand **80–89%**: Argentina, Ecuador, Uruguay, Malaysia, Singapore, Taiwan (China), Kuwait, Turkey, Denmark, Estonia, the United Kingdom, Croatia, Malta, Slovenia, Czech Republic, the Netherlands, Switzerland **70–80%**: Russian Federation, Poland, Romania, Slovakia **50–70%**: China, Mauritius, Bulgaria, Thailand **<50%**: India
Brain (adults)	**+6–10%**: USA, China, Republic of Korea, Singapore, Denmark, Estonia, Ireland, the United Kingdom, Malta, Spain, the Netherlands, Australia **+3–5%**: Martinique, Canada, Israel, Iceland, Latvia, Norway, Sweden, Croatia, Italy, France, Switzerland, New Zealand	**>40%**: Croatia **30–40%**: Canada, USA, Puerto Rico, Martinique, Singapore, China, Republic of Korea, Israel, Kuwait, Turkey, Denmark, Estonia, Finland, Ireland, Norway, Sweden, Belgium, Germany, Switzerland, Australia **20–29%**: Chile, Ecuador, Taiwan (China), Iceland, Latvia, the United Kingdom, Italy, Malta, Portugal, Slovenia, Spain, Czech Republic, Poland, Russian Federation, Slovakia, Austria, France, the Netherlands, New Zealand **14.7%**: Thailand

Site	Absolute percentage increase in survival rate 2000–2004 and 2010–2014	Survival rate 2010–2014
Myeloid malignancies	**+20–30%**: Lithuania, Sweden **+10–20%**: Czech Republic, Republic of Korea, Denmark, Netherlands, Norway **+5–10%**: USA, China, Taiwan (China), Japan, Singapore, Ireland, the United Kingdom, Portugal, Spain, Poland, Austria, Belgium, Germany, Australia	**55–60%**: Belgium, France, Germany, Sweden **50–54%**: Canada, Turkey, Ireland, Lithuania, Norway, Portugal, Spain, Romania, the Netherlands, Switzerland, Australia **40–49%**: USA, Martinique, Puerto Rico, Israel, Republic of Korea, Singapore, Denmark, Iceland, the United Kingdom, Italy, New Zealand **30–39%**: Argentina, Brazil, Japan, Malaysia, Taiwan (China), Estonia, Croatia, Slovenia, Czech Republic, Russian Federation, Slovakia, Austria **<30%**: Chile, Ecuador, China, Kuwait, Thailand, Latvia, Poland
Lymphoid malignancies	**+>10%**: Puerto Rico, Republic of Korea, Kuwait, Singapore, Denmark, Ireland, Latvia, Lithuania, Norway, the United Kingdom, Malta, Poland, the Netherlands, Switzerland **+5–10%**: Ecuador, Canada, USA, Japan, Taiwan (China), Finland, Estonia, Iceland, Sweden, Croatia, Portugal, Slovenia, Bulgaria, Czech Republic, Russian Federation, Slovakia, Austria, Belgium, France, Germany, Australia, New Zealand	**>70%**: Denmark, Iceland, Latvia, Belgium, France, Switzerland, Australia **60–69%**: Mauritius, Puerto Rico, Canada, USA, Israel, Kuwait, Finland, Ireland, Norway, Sweden, the United Kingdom, Italy, Malta, Portugal, Spain, Austria, Germany, the Netherlands, New Zealand **50–59%**: Costa Rica, Malaysia, Singapore, Japan, Republic of Korea, Taiwan (China), Turkey, Estonia, Lithuania, Croatia, Slovenia, Czech Republic, Poland, Slovakia **<50%**: Argentina, Brazil, Chile, Ecuador, Martinique, China, India, Thailand, Bulgaria, Romania, Russian Federation
Brain (children)	**+>10%**: Denmark, Lithuania, Czech Republic, Slovakia **+5–10%**: USA, China, Republic of Korea, Turkey, Ireland, Croatia, Italy, Portugal, Germany, the Netherlands, Australia	**80%**: Denmark, Slovakia, Sweden **70–79%**: Canada, USA, Costa Rica, Puerto Rico, Israel, Japan, Finland, Ireland, Norway, the United Kingdom, Croatia, Italy, Portugal, Czech Republic, Belgium, France, Germany, Switzerland **60–69%**: Republic of Korea, Singapore, Turkey, Estonia, Latvia, Lithuania, Greece, Slovenia, Spain, Belarus, Poland, Russian Federation, the Netherlands, Australia **<40%**: Brazil, Mexico
Acute lymphoblastic leukaemia (children)	**+>10%**: Colombia, China, Taiwan (China), Japan, Republic of Korea, Turkey, Finland, Lithuania, the United Kingdom, Portugal, Spain, Belarus, Bulgaria, Belgium	**80–89%**: Costa Rica, Singapore, Japan, Republic of Korea, Israel, Kuwait, Turkey, Estonia, Ireland, Latvia, Norway, Sweden, Croatia, Greece, Italy, Spain, Belarus, Czech Republic, Poland, Slovakia, France **60–70%**: Brazil, Chile, Colombia, Peru **<60%**: China, Ecuador, Mexico

Site	Absolute percentage increase in survival rate 2000–2004 and 2010–2014	Survival rate 2010–2014
Lymphoma (children)	**+>20%**: Slovenia, Russian Federation **+10–20%**: Brazil, Bulgaria, Croatia, Poland **+5–10%**: USA, Republic of Korea, Singapore, Taiwan (China), the United Kingdom, Lithuania, Portugal, Spain, Slovakia, Germany	**>90%**: Canada, USA, Costa Rica, Puerto Rico, Singapore, Japan, Republic of Korea, Israel, Kuwait, Denmark, Finland, Ireland, Lithuania, Norway, the United Kingdom, Croatia, Italy, Portugal, Slovenia, Spain, Czech Republic, Poland, Russian Federation, Belgium, France, Germany, Switzerland, Australia, New Zealand **<70%**: Ecuador, China

Appendix C: Members of informal advisory groups

Essential Medicines List Cancer Medicines Working Group

Name	Country	Affiliation
Zeba AZIZ	Pakistan	Hameed Latif Hospital
Jolanta BILIŃSKA	Poland	Jonscher Hospital, Lodz, Poland
Christopher BOOTH	Canada	Kingston Health Sciences Centre
María Elena CABRERA CONTRERAS	Chile	Department of Internal Medicine East University of Chile
Franco CAVALLI	Switzerland	Oncology Institute of Southern Switzerland, Hospital San Giovanni
Noreen CHAN	Singapore	National University Cancer Institute
Elisabeth G.E. DE VRIES	Netherlands	University of Groningen
Tito A. FOJO	United States of America	Herbert Irving Pavilion, Columbia University, Department of Surgery
James LOVE	United States of America	Knowledge Ecology International
Keymanthri MOODLEY	South Africa	Centre for Medical Ethics and Law
Sumitra THONGPRASERT	Thailand	Faculty of Medicine, Chiang Mai University
Verna Dnk VANDERPUYE	Ghana	National Center for Radiotherapy, Korle Bu Teaching Hospital

Informal Advisory Group on the Pricing of Cancer Medicines

Name	**Country**	**Affiliation**
Kamaruzaman BIN SALEH	Malaysia	Ministry of Health (Kementerian Kesihatan Malaysia)
Moses CHISALE	Malawi	Central Medical Stores Trust
Avram DENBURG	Canada	University of Toronto and The Hospital for Sick Children (SickKids)
Gihan Hamdy EL-SISI	Egypt	The Ministry of Health and Population
Saad JADDOUA	Jordan	King Hussein Cancer Center
Jinsoo LEE	Republic of Korea	Korea National Cancer Center
Miriam NAARENDORP	Suriname	Ministry of Health (Ministerie van Volksgezondheid)
Sakthivel SELVERAJ	India	Public Health Foundation of India
Netnapis SUCHONWANICH	Thailand	National Health Security Office
Richard SULLIVAN	The United Kingdom	Institute of Cancer Policy, Kings College London
Fatima SULEMAN	South Africa	University of KwaZulu-Natal
Fola TAYO	Nigeria	Caleb University
Sabine VOGLER	Austria	Gesundheit Österreich GmbH WHO Collaborating Centre for Pharmaceutical Pricing and Reimbursement Policies
Andrew WILSON	Australia	Australian Government Department of Health

Appendix D: List of key publications relating to reviews of medicine pricing

First author (year)	Pricing approaches discussed	Country or region in scope
WHO (2015)[xxiv]	- Mark-up control - Tax exemptions and reductions - Cost-plus pricing - Internal and external reference pricing - Health technology assessments	Global
OECD (2008)[xxv]	- Mark-up control - Internal and external reference pricing - Market-based pricing - Cost-plus pricing - Procurement and tendering - Managed entry agreements	OECD countries
Panteli et al. (2016)[xxvi]	- Free pricing - External reference pricing - Internal reference pricing - Value-based pricing - Negotiations and tendering - Managed entry agreements - Patient cost-sharing	15 European countries
Schneider et al. (2017)[xxvii] Kavanos et al. (2017)[xxviii]	- External reference pricing	European countries, Brazil, Egypt, Jordan, Kuwait, Lebanon, Qatar, Saudi Arabia, South Africa, Republic of Korea and the United Arab Emirates
Towse et al. (2015)[xxix] Kaló et al. (2013)[xxx]	- Differential pricing	European Union Lower-income European countries
Clark et al. (2012)	- Tendering and negotiations	Global, with a focus on low- and middle-income countries

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[xxiv] WHO guideline on country pharmaceutical pricing policies. Geneva: World Health Organization; 2015 (http://apps.who.int/medicinedocs/documents/s21016en/s21016en.pdf, accessed 14 November 2018).

[xxv] Pharmaceutical pricing policies in a global market. Paris: Organisation for Economic Co-operation and Development; 2008 (http://www.oecd-ilibrary.org/social-issues-migration-health/pharmaceutical-pricing-policies-in-a-global-market_9789264044159-en, accessed 15 November 2018)

[xxvi] Panteli D, Arickx F, Cleemput I, Dedet G, Eckhardt H, Fogarty E, et al. Pharmaceutical regulation in 15 European countries: A review. Health Syst Transit. 2016;18(5):1–118.

[xxvii] Schneider P, Habl C, Németh G, Primožič S, Šebesta R. Best practice report on external reference pricing (ERP). EURIPID. 2017;2.

[xxviii] Kanavos P, Fontrier A-M, Gill J, Kyriopoulos D. The implementation of external reference pricing within and across country borders. London: London School of Economics; 2017 (http://www.lse.ac.uk/business-and-consultancy/consulting/assets/documents/the-implementation-of-external-reference-pricing-within-and-across-country-borders.pdf, accessed 14 November 2018).

[xxix] Towse A, Pistollato M, Mestre-Ferrandiz J, Khan Z, Kaura S, Garrison L. European Union pharmaceutical markets: a case for differential pricing? Int J Econ Bus. 2015;22(2):263–75.

[xxx] Kaló Z, Annemans L, Garrison LP. Differential pricing of new pharmaceuticals in lower income European countries. Expert Rev Pharmacoeconomics Outcomes Res. 2013;13(6):735–41.

Appendix E: Health expenditure on pharmaceuticals and disease burden

Fig. E.1: Proportion of total health expenditure on spending of pharmaceuticals

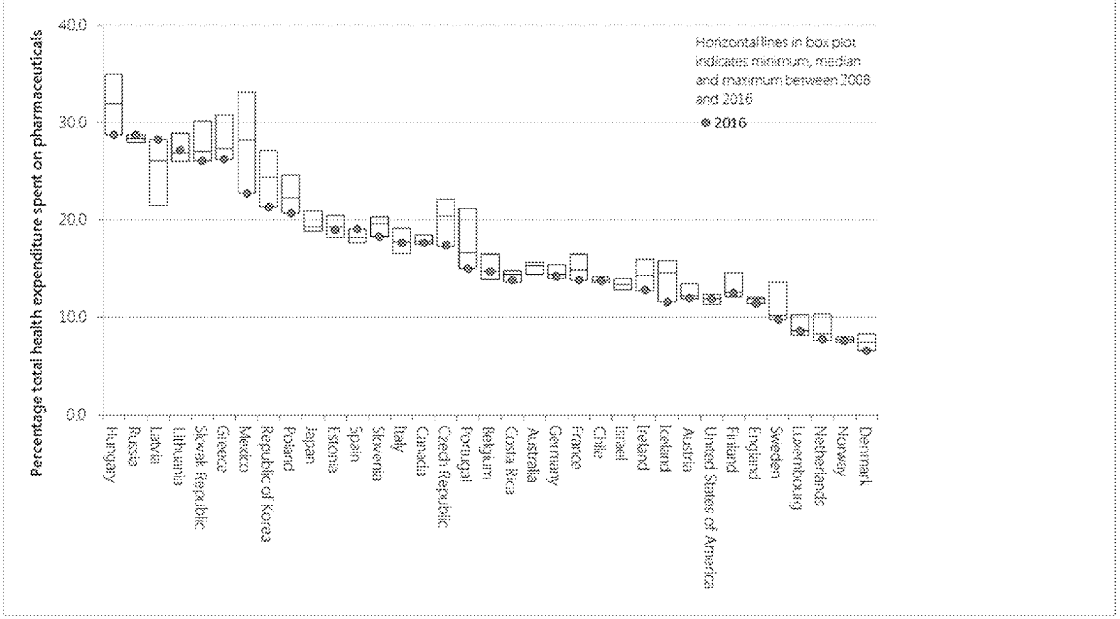
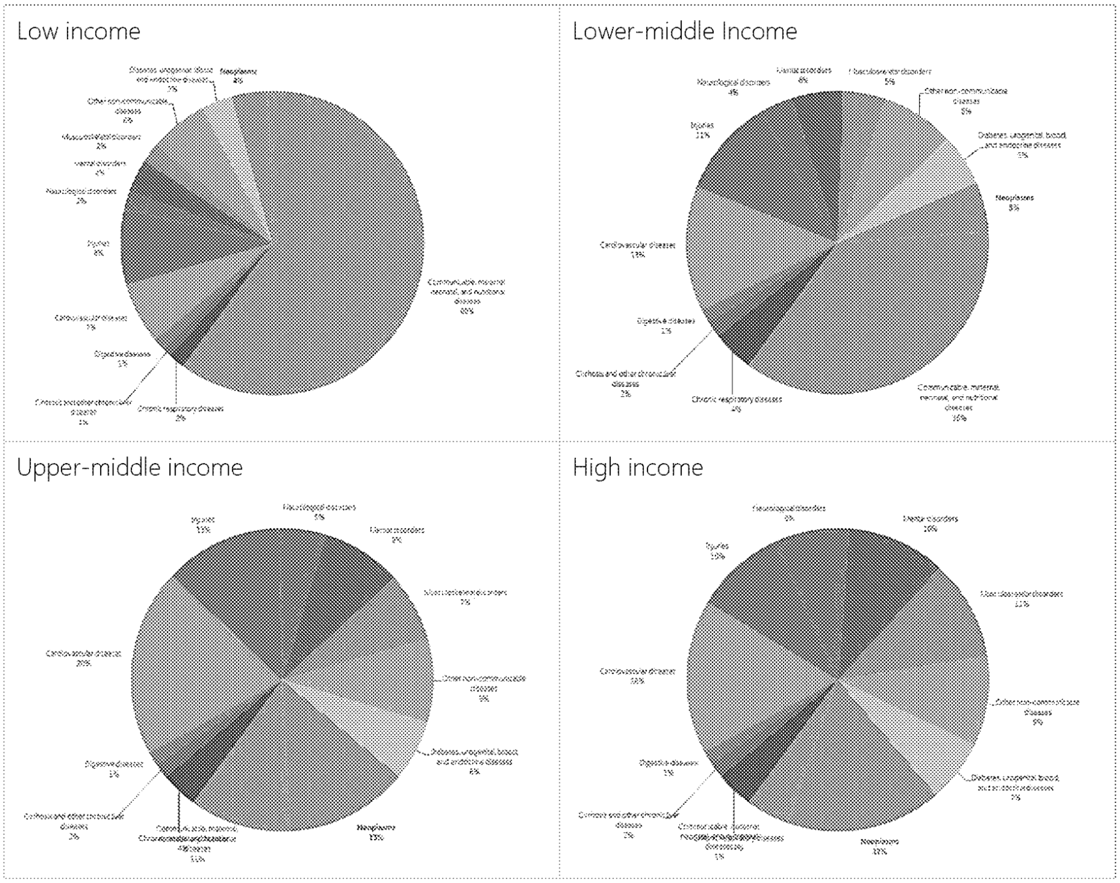
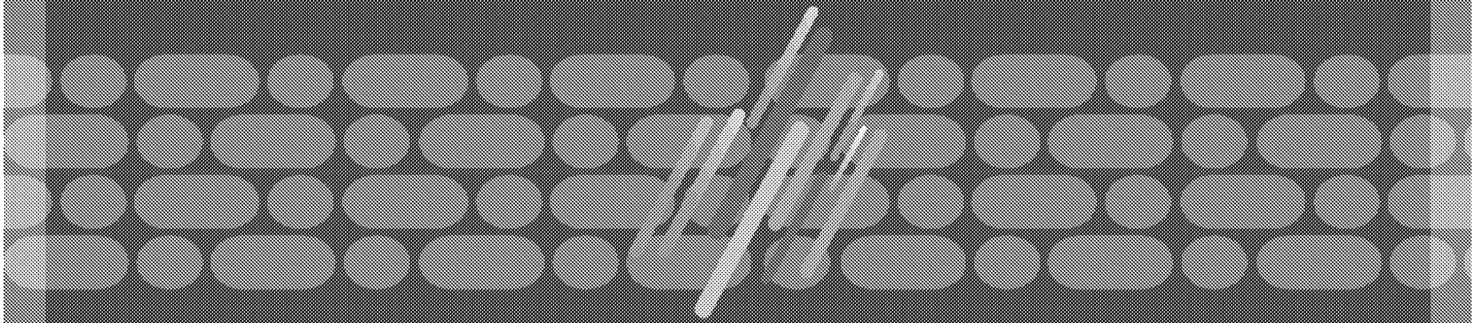


Fig. E.2: Proportion of DALYs by disease area and country income level





ISBN 978-92-4-151511-5

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From: Wolinetz, Carrie (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=WOLINETZCDC9A]
Sent: 10/21/2016 12:14:47 AM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]
Subject: RE: Request for Mtg on Xtandi for Export to Developing Countries

Mark,

Did you and Ann and Dale meet yesterday? What is the status of the meeting with KEI or response to the Secretary's letter? Cheers, Carrie

---

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Tuesday, October 18, 2016 10:27 AM
To: Wolinetz, Carrie (NIH/OD) [E]; Myles, Renate (NIH/OD) [E]; Burklow, John (NIH/OD) [E]; Hammersla, Ann (NIH/OD) [E]
Subject: FW: Request for Mtg on Xtandi for Export to Developing Countries

Peter Mamacos from OGA/HHS called me yesterday to ask b5 b5 He mentioned in passing that it would be b5 b5 Is that a possibility b5 b5

From: Bleimund, Emily (OS/OGA)
Sent: Tuesday, October 18, 2016 10:15 AM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>; Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Cc: Bulls, Michelle G. (NIH/OD) [E] <michelle.bulls@nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>; Wolinetz, Carrie (NIH/OD) [E] <carrie.wolinetz@nih.gov>; Snyder, Anne (HHS/OS/OGA) <Anne.Snyder@hhs.gov>
Subject: RE: Request for Mtg on Xtandi for Export to Developing Countries

FYI article today from IP-Watch...

http://www.ip-watch.org/2016/10/17/55-civil-society-groups-ask-us-government-to-allow-export-of-affordable-version-of-prostate-cancer-drug-xtandi/?utm_source=IP-Watch+Subscribers&utm_campaign=a91e0807a7-DAILY_SUMMARY&utm_medium=email&utm_term=0_b78685696b-a91e0807a7-352140865

55 Civil Society Groups Ask US Government To Allow Export Of Affordable Version Of Prostate Cancer Drug Xtandi

17/10/2016 by Intellectual Property Watch 1 Comment

A range of 55 civil society organisations from around the world today sent a letter asking the United States Department of Health and Human Services to accept an offer from a Canadian generics company, Biolyse Pharma, to manufacture and export high-priced cancer drug Xtandi to countries with a per capita income of less than one-third that of the United States.

The groups included Knowledge Ecology International, Public Citizen, Oxfam, NAACP, cancer and HIV/AIDS groups and "a host of other social justice, faith, patient, and consumer groups," as described by KEI in a release.

The letter and press statements are here: http://keionline.org/node/2645

According to KEI, Biolyse asked the US to enter into an agreement by exercising its royalty-free licence rights under the Bayh-Dole Act, which allows the government to use taxpayer-funded patented inventions "for or on behalf" of the United States.

The cancer drug enzalutamide, with the brand name Xtandi, was developed with US government funding.

"Xtandi is sold in the United States at a price of over $129,000 per year, by two drug companies: California-based Medivation, which has a licensing deal on the drug with UCLA, and Japan-based Astellas," according to the letter.

"Pfizer announced in August that it would purchase Medivation for $14 billion, just months after UCLA sold its royalty rights for Xtandi for over $1 billion. Xtandi is already in the top 10 cancer drugs for worldwide revenue, and is expected to move up to the top 5 by 2021," it said.

The letter said that whether the US government enters into agreement with Biolyse or other generics producers, the drug "will be far less expensive and far more widely accessible."

"Often neglected in the US drug pricing debate is the power the government has to protect the public from excessive prices for drugs that were developed with federal research funding," KEI Director James Love said in a statement. "While some might accept that the United States will tolerate excessively high domestic prices on a federally funded invention, it is an entirely different matter to ignore the consequences of high prices in countries where incomes are far lower."

Emily Bleimund, JD, MA
Director, Office of Trade and Health
Office of Global Affairs
U.S. Department of Health and Human Services
202-691-2188
Mobile b6
www.hhs.gov/global

From: Hammersla, Ann (NIH/OD) [E] [mailto:hammerslaa@mail.nih.gov]
Sent: Monday, October 17, 2016 2:17 PM
To: Bleimund, Emily (OS/OGA); Berkley, Dale (NIH/OD) [E]
Cc: Bulls, Michelle G. (NIH/OD) [E]; Rohrbaugh, Mark (NIH/OD) [E]; Wolinetz, Carrie (NIH/OD) [E]
Subject: RE: Request for Mtg on Xtandi for Export to Developing Countries

All:

I just sent a meeting request for Emily, Dale and Mark and I to meet to understand more of the background and requests by KEI for Wednesday.

Ann

From: Bleimund, Emily (OS/OGA)
Sent: Monday, October 17, 2016 12:53 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>; Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>
Cc: Bulls, Michelle G. (NIH/OD) [E] <michelle.bulls@nih.gov>; Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>; Wolinetz, Carrie (NIH/OD) [E] <carrie.wolinetz@nih.gov>
Subject: RE: Request for Mtg on Xtandi for Export to Developing Countries

Hi all – I'm just following up on this as KEI staff just called me at the office to ask again if we can meet, and also sent yet another letter today signed by 54 cancer organizations (see attached). b5 b5 but I want to make sure I'm coordinated with you all on this.

Emily

Emily Bleimund, JD, MA
Director, Office of Trade and Health
Office of Global Affairs
U.S. Department of Health and Human Services
202-691-2188
Mobile b6
www.hhs.gov/global

From: Bleimund, Emily (OS/OGA)
Sent: Thursday, October 13, 2016 1:09 PM
To: Hammersla, Ann (NIH/OD) [E]; Berkley, Dale (NIH/OD) [E]
Cc: Bulls, Michelle G. (NIH/OD) [E]; Rohrbaugh, Mark (NIH/OD) [E]; Wolinetz, Carrie (NIH/OD) [E]
Subject: Re: Request for Mtg on Xtandi for Export to Developing Countries

Thanks Ann. Let me know when is a good time for you all.

Emily

Emily Bleimund, JD, MA
Director, Office of Trade and Health
Office of Global Affairs –International Health Action for a Healthier US
U.S. Department of Health and Human Services
202-691-2188
Mobile b6
>www.globalhealth.gov<

From: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Sent: Wednesday, October 12, 2016 4:15:12 PM
To: Bleimund, Emily (OS/OGA); Berkley, Dale (NIH/OD) [E]
Cc: Bulls, Michelle G. (NIH/OD) [E]; Rohrbaugh, Mark (NIH/OD) [E]; Wolinetz, Carrie (NIH/OD) [E]
Subject: RE: Request for Mtg on Xtandi for Export to Developing Countries

Dear Emily:

As Dale indicated below a staff meeting may be possible. b5
b5

As a follow-up I will arrange a meeting so that we can discuss this possibility. b5
b5

Ann

From: Bleimund, Emily (OS/OGA)
Sent: Wednesday, October 12, 2016 1:09 PM
To: Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>; Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: Fw: Request for Mtg on Xtandi for Export to Developing Countries

Dale/Ann,

Not sure who are the right folks on this, but I wanted to discuss the possibility with you of granting KEI a staff-level meeting on this issue. Their original request letter is attached. b5 b5 b5 Granting a staff-level meeting to allow them to make their points b5

Thoughts? Thanks.

Emily

Emily Bleimund, JD, MA
Director, Office of Trade and Health
Office of Global Affairs –International Health Action for a Healthier US
U.S. Department of Health and Human Services
202-691-2188
Mobile b6
>www.globalhealth.gov<

From: Paul Davis <pdavis@keionline.org>
Sent: Wednesday, October 12, 2016 10:00:51 AM
To: Paul Davis
Cc: Burwell, Sylvia M. (HHS/OS); Kolker, Jimmy (HHS/OGA); Bleimund, Emily (OS/OGA); James Packard Love
Subject: Re: Request for Mtg on Xtandi for Export to Developing Countries

Dear Colleagues,

A few of us would appreciate the opportunity to have a word with you on this. Please let us know of any availability in the next couple weeks.

Thank you.

—
Paul Davis • pdavis@keionline.org
Knowledge Ecology Int'l
+1 202 817 0129
Skype/IM: pdavisx

> On Oct 5, 2016, at 11:47 AM, Paul Davis <pdavis@keionline.org> wrote:
>
> [Apologies for partial subject line in previous email.]
>
> 5 October, 2016
>
> The Honorable Sylvia Mary Mathews Burwell
> Secretary, Department of Health and Human Services
> 200 Independence Avenue, S.W.
> Washington, D.C. 20201
>
> Dear Secretary Burwell,
>
> Your office has received an important letter from the Canadian company Biolyse Pharma,

requesting that the United States exercise its rights to grant permission to manufacture enzalutamide for export to developing countries. The drug is marketed as Xtandi by Astellas Pharma.

Xtandi is an important drug—and one that was invented substantially with public funds. The prices set by Astellas deny access to almost everyone in need worldwide.

Advanced prostate cancer is a devastating disease--and one that is growing quickly in emerging economies. When this fact is coupled with the severely disproportionate rates of mortality documented in patients of African descent, we see an unacceptable status quo that requires a response. Fortunately, ready solutions are at hand.

Knowledge Economy International requests a meeting between you and your staff to discuss the Biolyse letter and move towards actions that can be taken to increase access to enzalutamide in developing countries. Is there a time in the coming weeks we can meet?

Thank you.

Paul Davis, Knowledge Ecology International

Enclosures: 28 Sept Letter to DHHS from Biolyse Pharma

CC: Amb Jimmy Kolker, Assistant Secretary for Global Affairs
Emily Bleimund, Director, Office of Trade and Health

—
Paul Davis
pdavis@keionline.org
Knowledge Ecology Int’l
+1 202 817 0129
Skype/IM: pdavisx

<Biolyse Letter 28 Aug 2016.pdf>

From: Hammersla, Ann (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=RECIPIENTS/CN=HAMMERSLAA]
Sent: 10/12/2016 8:13:46 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]; Wolinetz, Carrie (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Wolinetzcdc9a]; Bulls, Michelle G. (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Bullsmg]
Subject: FW: Request for Mtg on Xtandi for Export to Developing Countries

It is also b5
b5 .. See my next email.

From: Hammersla, Ann (NIH/OD) [E]
Sent: Wednesday, October 12, 2016 4:12 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Cc: Wolinetz, Carrie (NIH/OD) [E] <carrie.wolinetz@nih.gov>
Subject: RE: Request for Mtg on Xtandi for Export to Developing Countries

b5

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, October 12, 2016 4:11 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Cc: Wolinetz, Carrie (NIH/OD) [E] <carrie.wolinetz@nih.gov>
Subject: Re: Request for Mtg on Xtandi for Export to Developing Countries

I think b5
b5

Sent from my iPhone

On Oct 12, 2016, at 2:21 PM, Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov> wrote:

> **From:** Berkley, Dale (NIH/OD) [E]
> **Sent:** Wednesday, October 12, 2016 1:24 PM
> **To:** Bleimund, Emily (OS/OGA) <Emily.Bleimund@hhs.gov>; Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
> **Subject:** RE: Request for Mtg on Xtandi for Export to Developing Countries
>
> Emily:
>
> This is b5
> b5
> b5
>
> I'm sure Ann can arrange to get the right people at NIH to look at your question.
>
> Best, Dale

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
301-496-6043
301-402-2528(Fax)

This message is intended for the exclusive use of the recipient(s) named above. It may contain information that is PROTECTED or PRIVILEGED, and it should not be disseminated, distributed, or copied to persons not authorized to receive such information.

From: Bleimund, Emily (OS/OGA)
Sent: Wednesday, October 12, 2016 1:09 PM
To: Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>; Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: Fw: Request for Mtg on Xtandi for Export to Developing Countries

Dale/Ann,

Not sure who are the right folks on this, but I wanted to discuss the possibility with you of granting KEI a staff-level meeting on this issue. Their original request letter is attached. b5
b5
b5 Granting a staff-level meeting to allow them to make their points b5

Thoughts? Thanks.

Emily

Emily Bleimund, JD, MA
Director, Office of Trade and Health
Office of Global Affairs –International Health Action for a Healthier US
U.S. Department of Health and Human Services
202-691-2188
Mobile: b6
>www.globalhealth.gov<

From: Paul Davis <pdavis@keionline.org>
Sent: Wednesday, October 12, 2016 10:00:51 AM
To: Paul Davis
Cc: Burwell, Sylvia M. (HHS/OS); Kolker, Jimmy (HHS/OGA); Bleimund, Emily (OS/OGA); James Packard Love
Subject: Re: Request for Mtg on Xtandi for Export to Developing Countries

Dear Colleagues,

A few of us would appreciate the opportunity to have a word with you on this. Please let us know of any availability in the next couple weeks.

Thank you.

—
Paul Davis • pdavis@keionline.org
Knowledge Ecology Int'l

+1 202 817 0129
Skype/IM: pdavisx

On Oct 5, 2016, at 11:47 AM, Paul Davis <pdavis@keionline.org> wrote:

[Apologies for partial subject line in previous email.]

5 October, 2016

The Honorable Sylvia Mary Mathews Burwell
Secretary, Department of Health and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201

Dear Secretary Burwell,

Your office has received an important letter from the Canadian company Biolyse Pharma, requesting that the United States exercise its rights to grant permission to manufacture enzalutamide for export to developing countries. The drug is marketed as Xtandi by Astellas Pharma.

Xtandi is an important drug—and one that was invented substantially with public funds. The prices set by Astellas deny access to almost everyone in need worldwide.

Advanced prostate cancer is a devastating disease--and one that is growing quickly in emerging economies. When this fact is coupled with the severely disproportionate rates of mortality documented in patients of African descent, we see an unacceptable status quo that requires a response. Fortunately, ready solutions are at hand.

Knowledge Economy International requests a meeting between you and your staff to discuss the Biolyse letter and move towards actions that can be taken to increase access to enzalutamide in developing countries. Is there a time in the coming weeks we can meet?

Thank you.

Paul Davis, Knowledge Ecology International

Enclosures: 28 Sept Letter to DHHS from Biolyse Pharma

CC: Amb Jimmy Kolker, Assistant Secretary for Global Affairs
Emily Bleimund, Director, Office of Trade and Health

—
Paul Davis
pdavis@keionline.org
Knowledge Ecology Int’l
+1 202 817 0129
Skype/IM: pdavisx

<Biolyse Letter 28 Aug 2016.pdf>

From: Hammersla, Ann (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=RECIPIENTS/CN=HAMMERSLAA]
Sent: 10/12/2016 8:07:21 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=OD/cn=ROHRBAUM]; Wolinetz, Carrie (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Wolinetzcdc9a]; Bulls, Michelle G. (NIH/OD) [E] [/O=NIH/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=Bullsmg]
Subject: RE: Request for Mtg on Xtandi for Export to Developing Countries

It is unclear to me b5 The request is b5 b5 I am assuming b5 b5

From: Rohrbaugh, Mark (NIH/OD) [E]
Sent: Wednesday, October 12, 2016 2:31 PM
To: Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>; Wolinetz, Carrie (NIH/OD) [E] <carrie.wolinetz@nih.gov>
Subject: RE: Request for Mtg on Xtandi for Export to Developing Countries

Is b5 in my opinion or b5

From: Hammersla, Ann (NIH/OD) [E]
Sent: Wednesday, October 12, 2016 2:22 PM
To: Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>
Subject: FW: Request for Mtg on Xtandi for Export to Developing Countries

---

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Sent: Wednesday, October 12, 2016 1:24 PM
To: Bleimund, Emily (OS/OGA) <Emily.Bleimund@hhs.gov>; Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: RE: Request for Mtg on Xtandi for Export to Developing Countries

Emily:

This is b5 b5

I'm sure Ann can arrange to get the right people at NIH to look at your question.

Best, Dale

Dale D. Berkley, Ph.D., J.D.
Office of the General Counsel, PHD, NIH Branch
Bldg. 31, Rm. 47
Bethesda, MD 20892
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Thoughts? Thanks.

Emily

Emily Bleimund, JD, MA
Director, Office of Trade and Health
Office of Global Affairs –International Health Action for a Healthier US
U.S. Department of Health and Human Services
202-691-2188
Mobile b6
>www.globalhealth.gov<

From: Paul Davis <pdavis@keionline.org>
Sent: Wednesday, October 12, 2016 10:00:51 AM
To: Paul Davis
Cc: Burwell, Sylvia M. (HHS/OS); Kolker, Jimmy (HHS/OGA); Bleimund, Emily (OS/OGA); James Packard Love
Subject: Re: Request for Mtg on Xtandi for Export to Developing Countries

Dear Colleagues,

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Paul Davis • pdavis@keionline.org
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+1 202 817 0129
Skype/IM: pdavisx

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>
> 5 October, 2016
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200 Independence Avenue, S.W.
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Thank you.

Paul Davis, Knowledge Ecology International

Enclosures: 28 Sept Letter to DHHS from Biolyse Pharma

CC: Amb Jimmy Kolker, Assistant Secretary for Global Affairs
Emily Bleimund, Director, Office of Trade and Health

—
Paul Davis
pdavis@keionline.org
Knowledge Ecology Int'l
+1 202 817 0129
Skype/IM: pdavisx

<Biolyse Letter 28 Aug 2016.pdf>

From: Snyder, Anne (HHS/OS/OGA) [Anne.Snyder@hhs.gov]
Sent: 1/4/2019 5:18:13 PM
To: Eiss, Robert (NIH/FIC) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=707887ee7ba548e1a0ae55f683ce2017-eissr]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: FW: Please review: WHO technical report on pricing of cancer medicine
Attachments: Pricing of Cancer Medicines and its impacts.pdf

Hi Rob/Mark-

Happy New Year to you both! I just wanted to bring this report up to the top of your inbox—given how technical this report is, it would really help to have NIH's feedback on the report to keep in mind as we draft the U.S. position paper in the next couple days. Have you all had a chance to review it? Please feel free to send it to other relevant offices as well.

I would particularly call your attention to pages 10-15 and 83-89, although there are other relevant sections too.

Best,

Anne Snyder, J.D.
Global Health Officer, Trade and Health
Office of Global Affairs
U.S. Department of Health and Human Services
hhs.gov/global

P: 202-260-0415
M: b6

From: Snyder, Anne (HHS/OS/OGA)
Sent: Wednesday, December 19, 2018 1:34 PM
To: Kerr, Lawrence (HHS/OS/OGA) <Lawrence.Kerr@hhs.gov>; Filpi, Lynn (HHS/OS/OGA) <Lynn.Filpi@hhs.gov>; Weinberger, Collin (OS/OGA) (CTR) <Collin.Weinberger@hhs.gov>; Abdoo, Mark (FDA/OC) <Mark.Abdoo@fda.hhs.gov>; Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>; Eiss, Robert (NIH/FIC) [E] <eissr@mail.nih.gov>; Berliner, Elise (AHRQ/CEPI) <Elise.Berliner@ahrq.hhs.gov>; CGH/OD Policy Office Inbox (CDC.GOV) <cghpolicyrequests@cdc.gov>; Bush, Laina (HHS/ASPE) <Laina.Bush@HHS.GOV>; Hsu-Luftman, Leah (FDA/OC) (Leah.Luftman@fda.hhs.gov) <Leah.Luftman@fda.hhs.gov>; Valdez, Mary Lou (FDA/OC) <MaryLou.Valdez@fda.hhs.gov>; Talley, Rose M. (CMS/OSORA) <Rose.Talley@cms.hhs.gov>; Delew, Nancy (HHS/ASPE) <Nancy.Delew@hhs.gov>
Cc: Bleimund, Emily (OS/OGA) <Emily.Bleimund@hhs.gov>; Danelski, Ann (HHS/OGA) <Ann.Danelski@hhs.gov>; Schmeissner, Peter (HHS/OGA) <Peter.Schmeissner@hhs.gov>; Lamourelle, Gabrielle (HHS/OS/OGA) <Gabrielle.Lamourelle@hhs.gov>; 'Carson, Tracy L (Geneva)' <CarsonTL@state.gov>; Stewart, Jessica L. (HHS/OS/OGA) <Jessica.Stewart@hhs.gov>; Mciff, Colin (HHS/OS/OGA) <Colin.Mciff@hhs.gov>; 'Smith, Sean R (Geneva)' <SmithSR1@state.gov>; 'McPhee, Megan E (Geneva)' <McPheeME@state.gov>
Subject: Please review: WHO technical report on pricing of cancer medicine

Dear colleagues-

Last night, WHO released a much-anticipated technical report on "Pricing of cancer medicines and its impacts". This report was requested by the 70th World Health Assembly in 2017, (http://apps.who.int/gb/ebwha/pdf_files/WHA70/A70_R12-en.pdf?ua=1) and it will be discussed at the end of January at the WHO Executive Board under the same agenda item as the Roadmap on Access to Medicines. We expect that other Member States will be very interested in the report's findings.

OGA is still reviewing the technical report and will be preparing a position paper on it, which we expect to circulate for your review in January. However, we would also welcome feedback from HHS subject matter experts in the meantime—which hopefully will make the review process a bit easier after the New Year. Please send us any initial feedback you have by **COB on December 31st** to ensure that we are able to take it into account when drafting the position paper.

As always, please let me know if you have any questions.

Best,

Anne Snyder, J.D.
Global Health Officer, Trade and Health
Office of Global Affairs
U.S. Department of Health and Human Services
hhs.gov/global

P: 202-260-0415
M: b6

From: Eiss, Robert (NIH/FIC) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=707887EE7BA548E1A0AE55F683CE2017-EISSR]
Sent: 1/4/2019 5:36:34 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: Fwd: Please review: WHO technical report on pricing of cancer medicine
Attachments: Pricing of Cancer Medicines and its impacts.pdf; ATT00001.htm

Mark,

I skimmed this report but had not commented b5 b5 I can make comments b5 b5 any advice is valued

Sent from my iPhone

Begin forwarded message:

> **From:** "Snyder, Anne (HHS/OS/OGA)" <Anne.Snyder@hhs.gov>
> **To:** "Eiss, Robert (NIH/FIC) [E]" <eissr@mail.nih.gov>, "Rohrbaugh, Mark (NIH/OD) [E]" <rohrbaum@od.nih.gov>
> **Subject: FW: Please review: WHO technical report on pricing of cancer medicine**
>
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>
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> Anne Snyder, J.D.
> Global Health Officer, Trade and Health
> Office of Global Affairs
> U.S. Department of Health and Human Services
> hhs.gov/global
>
> P: 202-260-0415
> M: b6
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> **From:** Snyder, Anne (HHS/OS/OGA)
> **Sent:** Wednesday, December 19, 2018 1:34 PM
> **To:** Kerr, Lawrence (HHS/OS/OGA) <Lawrence.Kerr@hhs.gov>; Filpi, Lynn (HHS/OS/OGA) <Lynn.Filpi@hhs.gov>; Weinberger, Collin (OS/OGA) (CTR) <Collin.Weinberger@hhs.gov>; Abdoo, Mark (FDA/OC) <Mark.Abdoo@fda.hhs.gov>; Rohrbaugh, Mark (NIH/OD) [E] <RohrBauM@OD.NIH.GOV>; Eiss, Robert (NIH/FIC) [E] <eissr@mail.nih.gov>; Berliner, Elise (AHRQ/CEPI) <Elise.Berliner@ahrq.hhs.gov>; CGH/OD Policy Office Inbox (CDC.GOV) <cghpolicyrequests@cdc.gov>; Bush, Laina (HHS/ASPE)

<Laina.Bush@HHS.GOV>; Hsu-Luftman, Leah (FDA/OC) (Leah.Luftman@fda.hhs.gov) <Leah.Luftman@fda.hhs.gov>; Valdez, Mary Lou (FDA/OC) <MaryLou.Valdez@fda.hhs.gov>; Talley, Rose M. (CMS/OSORA) <Rose.Talley@cms.hhs.gov>; Delew, Nancy (HHS/ASPE) <Nancy.Delew@hhs.gov>
Cc: Bleimund, Emily (OS/OGA) <Emily.Bleimund@hhs.gov>; Danelski, Ann (HHS/OGA) <Ann.Danelski@hhs.gov>; Schmeissner, Peter (HHS/OGA) <Peter.Schmeissner@hhs.gov>; Lamourelle, Gabrielle (HHS/OS/OGA) <Gabrielle.Lamourelle@hhs.gov>; 'Carson, Tracy L (Geneva)' <CarsonTL@state.gov>; Stewart, Jessica L. (HHS/OS/OGA) <Jessica.Stewart@hhs.gov>; Mciff, Colin (HHS/OS/OGA) <Colin.Mciff@hhs.gov>; 'Smith, Sean R (Geneva)' <SmithSR1@state.gov>; 'McPhee, Megan E (Geneva)' <McPheeME@state.gov>
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As always, please let me know if you have any questions.

Best,

Anne Snyder, J.D.
Global Health Officer, Trade and Health
Office of Global Affairs
U.S. Department of Health and Human Services
hhs.gov/global

P: 202-260-0415
M b6

From: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=OD/CN=ROHRBAUM]
Sent: 11/2/2016 1:20:49 PM
To: Hammersla, Ann (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=Recipients/cn=hammerslaa]

Subject: Fwd: Meeting with NGOs on UN HLP
Attachments: UNSG+HLP+Report+FINAL+12+Sept+2016.pdf; ATT00001.htm
Location: 2322

Start: 11/4/2016 6:00:00 PM
End: 11/4/2016 7:00:00 PM
Show Time As: Tentative

Sent from my iPhone

Begin forwarded message:

> **From:** "Snyder, Anne (HHS/OS/OGA)" <Anne.Snyder@hhs.gov>
> **To:** "Bleimund, Emily (OS/OGA)" <Emily.Bleimund@hhs.gov>, "Mamacos, Peter (HHS/OGA)" <Peter.Mamacos@hhs.gov>, "Lamourelle, Gabrielle (HHS/OS/OGA)" <Gabrielle.Lamourelle@hhs.gov>, "Danelski, Ann (HHS/OGA)" <Ann.Danelski@hhs.gov>, "Wood, Rachel (HHS/OS/OGA)" <Rachel.Wood@hhs.gov>, "Kampf, Katie H. (HHS/OS/OGA)" <Katie.Kampf@hhs.gov>, "Wolfe, Mitchell (HHS/OS/OGA)" <Mitchell.Wolfe@hhs.gov>, "Schmeissner, Peter (HHS/OGA)" <Peter.Schmeissner@hhs.gov>, "Hoffman, Linda M (HHS/OS/OGA)" <Linda.Hoffman@hhs.gov>, "Kerr, Lawrence (HHS/OS/OGA)" <Lawrence.Kerr@hhs.gov>, "Abdoo, Mark (FDA/OC)" <Mark.Abdoo@fda.hhs.gov>, "Stewart, Jessica L. (HHS/OS/OGA)" <Jessica.Stewart@hhs.gov>, "Peters, Kenisha (HHS/OS/OGA) (CTR)" <Kenisha.Peters@hhs.gov>, "Rohrbaugh, Mark (NIH/OD) [E]" <RohrBauM@OD.NIH.GOV>, b6 (STATE.GOV)" b6 @state.gov>, ' b6 @state.gov>, "Wong, Holly (HHS/OS/OGA)" <Holly.Wong@hhs.gov>
> **Subject: Meeting with NGOs on UN HLP**
>
> *Corrected a typo in the conference call line*
>
> ***
>
> Hi all-
>
> A group of NGOs has requested to meet with OGA to present their views on the recently released Report of the UN High Level Panel on Access to Medicines. The final Report is attached to this meeting invite, and I have also included links to USG statements about the Report. We will mainly be in listening mode for the meeting, but please feel free to forward this email to others in HHS who should be included (and apologies if I inadvertently left anyone out). For those who cannot attend in person, we can use the following conference line.
>
> b6 (domestic)
> (international)
> Passcode: b6

Links to U.S. statements about the Panel/Report
U.S. submission to the Panel during its consultation period (prior to the release of the Report):
http://www.unsgaccessmeds.org/inbox/2016/2/27/united-states-department-of-state
U.S. statement upon the release of the Report:
https://www.state.gov/r/pa/prs/ps/2016/09/262034.htm

Best,

Anne Snyder, J.D.
Policy Analyst, Office of Trade and Health
Office of Global Affairs
U.S. Department of Health and Human Services
hhs.gov/global

P: 202-260-0415
M: b6

From: Rohrbaugh, Mark (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/CN=OD/CN=ROHRBAUM]
Sent: 10/13/2016 6:30:48 PM
To: Hammersla, Ann (NIH/OD) [E] [/O=NIH/OU=NIHEXCHANGE/cn=Recipients/cn=hammerslaa]
Subject: Fwd: Request for Mtg on Xtandi for Export to Developing Countries

I am available next week but not the following week

Sent from my iPhone

Begin forwarded message:

> **From:** "Bleimund, Emily (OS/OGA)" <Emily.Bleimund@hhs.gov>
> **Date:** October 13, 2016 at 1:08:30 PM EDT
> **To:** "Hammersla, Ann (NIH/OD) [E]" <hammerslaa@mail.nih.gov>, "Berkley, Dale (NIH/OD) [E]" <BerkleyD@OD.NIH.GOV>
> **Cc:** "Bulls, Michelle G. (NIH/OD) [E]" <michelle.bulls@nih.gov>, "Rohrbaugh, Mark (NIH/OD) [E]" <RohrBauM@OD.NIH.GOV>, "Wolinetz, Carrie (NIH/OD) [E]" <carrie.wolinetz@nih.gov>
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> Emily Bleimund, JD, MA
> Director, Office of Trade and Health
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> 202-691-2188
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>
> ---
>
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> **To:** Bleimund, Emily (OS/OGA); Berkley, Dale (NIH/OD) [E]
> **Cc:** Bulls, Michelle G. (NIH/OD) [E]; Rohrbaugh, Mark (NIH/OD) [E]; Wolinetz, Carrie (NIH/OD) [E]
> **Subject:** RE: Request for Mtg on Xtandi for Export to Developing Countries
>
> Dear Emily:
>
> As Dale indicated below a staff meeting may be possible. b5
> b5
>
> As a follow-up I will arrange a meeting so that we can discuss this possibility b5
> b5
>
> Ann

From: Bleimund, Emily (OS/OGA)
Sent: Wednesday, October 12, 2016 1:09 PM
To: Berkley, Dale (NIH/OD) [E] <BerkleyD@OD.NIH.GOV>; Hammersla, Ann (NIH/OD) [E] <hammerslaa@mail.nih.gov>
Subject: Fw: Request for Mtg on Xtandi for Export to Developing Countries

Dale/Ann,

Not sure who are the right folks on this, but I wanted to discuss the possibility with you of granting KEI a staff-level meeting on this issue. Their original request letter is attached. b5 b5 b5 Granting a staff-level meeting to allow them to make their points b5

Thoughts? Thanks.

Emily

Emily Bleimund, JD, MA
Director, Office of Trade and Health
Office of Global Affairs –International Health Action for a Healthier US
U.S. Department of Health and Human Services
202-691-2188
Mobile b6
>www.globalhealth.gov<

From: Paul Davis <pdavis@keionline.org>
Sent: Wednesday, October 12, 2016 10:00:51 AM
To: Paul Davis
Cc: Burwell, Sylvia M. (HHS/OS); Kolker, Jimmy (HHS/OGA); Bleimund, Emily (OS/OGA); James Packard Love
Subject: Re: Request for Mtg on Xtandi for Export to Developing Countries

Dear Colleagues,

A few of us would appreciate the opportunity to have a word with you on this. Please let us know of any availability in the next couple weeks.

Thank you.

—
Paul Davis • pdavis@keionline.org
Knowledge Ecology Int'l
+1 202 817 0129
Skype/IM: pdavisx

> On Oct 5, 2016, at 11:47 AM, Paul Davis <pdavis@keionline.org> wrote:
>
> [Apologies for partial subject line in previous email.]
>
> 5 October, 2016

The Honorable Sylvia Mary Mathews Burwell
Secretary, Department of Health and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201

Dear Secretary Burwell,

Your office has received an important letter from the Canadian company Biolyse Pharma, requesting that the United States exercise its rights to grant permission to manufacture enzalutamide for export to developing countries. The drug is marketed as Xtandi by Astellas Pharma.

Xtandi is an important drug—and one that was invented substantially with public funds. The prices set by Astellas deny access to almost everyone in need worldwide.

Advanced prostate cancer is a devastating disease--and one that is growing quickly in emerging economies. When this fact is coupled with the severely disproportionate rates of mortality documented in patients of African descent, we see an unacceptable status quo that requires a response. Fortunately, ready solutions are at hand.

Knowledge Economy International requests a meeting between you and your staff to discuss the Biolyse letter and move towards actions that can be taken to increase access to enzalutamide in developing countries. Is there a time in the coming weeks we can meet?

Thank you.

Paul Davis, Knowledge Ecology International

Enclosures: 28 Sept Letter to DHHS from Biolyse Pharma

CC: Amb Jimmy Kolker, Assistant Secretary for Global Affairs
Emily Bleimund, Director, Office of Trade and Health

—
Paul Davis
pdavis@keionline.org
Knowledge Ecology Int'l
+1 202 817 0129
Skype/IM: pdavisx

<Biolyse Letter 28 Aug 2016.pdf>

From: Bleimund, Emily (OS/OGA) [Emily.Bleimund@hhs.gov]
Sent: 3/14/2019 12:22:15 PM
To: Bleimund, Emily (OS/OGA) [Emily.Bleimund@hhs.gov]; Snyder, Anne (HHS/OS/OGA) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9ebb46d509b9437dac550d81d1dbc5ee-Anne.Berlow]; Danelski, Ann (HHS/OGA) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c210dc8082034d08956601d5e247ac3c-Ann.Danelsk]; Schmeissner, Peter (HHS/OGA) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=e3b014425a7b4630a9195705cc31e54e-Peter.Schme]; Lamourelle, Gabrielle (HHS/OS/OGA) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=217e0bf8b30b4548b8e2df338e59f156-Gabrie.Lamo]; Mciff, Colin (HHS/OS/OGA) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=1d549de9d75b456f9da4f1389650925e-Colin.Mciff]; Abdoo, Mark (FDA/OC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7eafb9b302054654ac154a0a334cc0a5-Mark.Abdoo.]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; Eiss, Robert (NIH/FIC) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=707887ee7ba548e1a0ae55f683ce2017-eissr]; b6 Aziz, Anjam EOP/USTR b6 Wang, Katherine E. EOP/UST b6 'Jennifer.Boger@trade.gov' [Jennifer.Boger@trade.gov]; Stevan Mitchell [Stevan.Mitchell@trade.gov]; Michael Finn (Michael.Finn@trade.gov) [Michael.Finn@trade.gov]; Rachel Salzman [Rachel.Salzman@trade.gov]; b6 b6 @state.gov]; b6 @state.gov' b6 @state.gov]; Lashley-Johnson, Deborah b6 Moezie, Minna F. [Minna.Moezie@USPTO.GOV]; Ferriter, Karin (Karin.Ferriter@USPTO.GOV) [Karin.Ferriter@USPTO.GOV]; Summer Kostelnik [Summer.Kostelnik@USPTO.GOV]; Won.Chang@treasury.gov; Megan Crowe [Megan.Crowe@trade.gov]; b6 @state.gov]; Susan Wilson [Susan.Wilson@trade.gov]; Huber, Valerie (HHS/OGA) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=df7c7b741f214f64ad0b55c4f39bf3a3-Valerie.Hub]
CC: Sorenson, Noila (OS/OGA) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d631e14a8b994d12b6c1c627e185ea23-Noila.Soren]

Subject: Italy transparency resolution
Attachments: italy-transparency-draft-resolution-020119.pdf; italy-transparency-letter-020119.pdf; draft_resolution transparency_72WHA COMBINED MARKUP 3-15-19.docx; Italy transparency resolution - IFPMA comments.pdf; Italy transparency resolution - PhRMA talking points (USG only).pdf; Italy transprency resolution - PhRMA track changes resolution text (USG only).pdf; Italy transparency resolution - PhRMA redlines (USG only).pdf; Open-Letter-WHA-Transparency-Resolution-6March2019.pdf
Location: T-con or HHS Humphrey Building 640H

Start: 3/18/2019 6:00:00 PM
End: 3/18/2019 7:00:00 PM
Show Time As: Busy

Recurrence: (none)

Also adding some feedback we have received from IFPMA and PhRMA, as well as a letter signed by 83 organizations and 20 individuals.

Adding combined markup of agency comments

Relevant documents again attached

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Confidential draft

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March 6, 2019

Open letter to WHO member states

On 1 February 2019, Italy submitted a draft resolution on transparency to the World Health Organization (WHO). This resolution is to be discussed in May 2019, at the 72nd session of the World Health Assembly (WHA).

The title of the proposed resolution is "Improving the transparency of markets for drugs, vaccines and other health-related technologies," and it sets out a number of measures designed to achieve this objective .

There are deplorable asymmetries of access to information about many aspects of the innovation and supply chain for medicines, vaccines and other health technologies. The lack of information creates confusion about basic facts related to prices, research and development costs and other aspects of the value chain for medicines, vaccines and health technologies.

The resolution would create a work program for the WHO and norms for governments to cooperate in improving the transparency of various aspects of these technologies.

This is a critical time for governments to consider reforms in pricing and incentives for innovation for health technologies. The transparency measures proposed in the resolution will ensure that consideration of such reforms will be based upon the best possible evidence.

We urge your government to support the resolution.

Organizations (in alphabetical order)

1. Access to Medicines Ireland (Ireland)
2. Accion Internacional para la Salud - Perú
3. Action against AIDS (Germany)
4. ACTION Global Health Advocacy Partnership (Global)
5. AIDES (France)
6. AIDS and Rights Alliance for Southern Africa (ARASA)
7. AIDS Healthcare Foundation (AHF) (US)
8. Alliance for Reproductive Health Rights (ARHR) (Ghana)
9. Associação Brasileira Interdisciplinar de AIDS (ABIA) (Brazil)
10. Ben Newman Hope Care Foundation (Ghana)
11. Botswana Network on Ethics, Law and HIV/AIDS (BONELA) (Botswana)
12. BUKO Pharma-Kampagne (Germany)
13. Cancer Alliance (South Africa)
14. Center for Health, Human Rights and Development (CEHURD) (Kampala, Uganda)

15. Centre for Community Studies, Action and Development (CENCOSAD) (Ghana)
16. Chasing Zero (UK)
17. Coalition Plus
18. Commons Network (EU)
19. Consumer Association the Quality of LIfe - EKPIZO (Greece)
20. Drug for Neglected Diseases Initiative (DNDi)
21. Empower India (India)
22. European Alliance for Responsible R&D and Affordable Medicines
23. European Public Health Alliance (EPHA)
24. France Assos Santé (France)
25. Global Health Advocates (France)
26. Global Justice Now (UK)
27. Groupe sida Genève - (Switzerland)
28. Grupo de Trabalho sobre Propriedade Intelectual (GTPI) (Brazil)
29. Health Action International (HAI)
30. Health Gap
31. Health Innovation in Practice (HIP)
32. Heart to Heart Foundation (Thailand)
33. Hepatitis Scotland (UK)
34. IFARMA Foundation (Colombia)
35. Interfaith Center for Corporate Responsibility (ICCR)(US)
36. International Treatment Preparedness Coalition (ITPC)
37. Just Treatment (UK)
38. KEI Europe (Switzerland)
39. Kenya Legal & Ethical Issues Network (KELIN) (Kenya)
40. Kenyan Network of Cancer Organizations (KENCO) (Kenya)
41. Knowledge Ecology International (KEI)
42. Korean Pharmacists for Democratic Society (KPDS) (South Korea)
43. Malawi Network of Religious Leaders Living with or Personally Affected by HIV and AIDS (MANERELA+) (Malawi)
44. Médecins du Monde International
45. Médecins Sans Frontières Access Campaign
46. Misión Salud (Colombia)
47. NCD Alliance East Africa (EANCDA)
48. Non Communicable Disease Alliance of Kenya (NCD-AK) (Kenya)
49. Oxfam
50. Pan African Positive Women's Coalition-Zimbabwe
51. Pan-African Treatment Access Movement (PATAM)
52. People's Health Institute (PHI) (South Korea)
53. People's Health Movement (PHM)
54. PHM East Africa
55. PHM Kenya
56. Positive Malaysian Treatment Access & Advocacy Group (MTAAG+) (Malaysia)

57. Prescrire (France)
58. Public Citizen (US)
59. Public Eye (Switzerland)
60. Réseau Accès aux Médicaments Essentiels (RAME) (Burkina Faso)
61. Salud por Derecho (Spain)
62. Salud y Farmacos (USA)
63. Save the Children
64. SECTION27 (South Africa)
65. Solthis (France)
66. Southern African Programme on Access to Medicines and Diagnostics
67. STOPAIDS (UK)
68. T1International
69. Tanzania Breast Cancer Foundation (Tanzania)
70. Third World Network (TWN)
71. Test Aankoop/Test Achats (Belgium)
72. Trans Atlantic Consumer Dialogue (TACD)
73. TranspariMED (UK)
74. Treatment Action Group (TAG) (United States)
75. Treatment Advocacy and Literacy Campaign (TALC) - Zambia
76. Uganda NCD Alliance (Uganda)
77. Union for Affordable Cancer Treatment (UACT)
78. Universal Access to Health Care Campaign (UAHCC) (Ghana)
79. Universities Allied for Essential Medicines (UAEM)
80. Wemos (Netherlands)
81. Women's Coalition Against Cancer (WOCACA) (Malawi)
82. Yolse (Switzerland)
83. Young Professionals Chronic Disease Network (YP-CDN)

Individuals (in alphabetical order)

1. Aidan Hollis, Professor of Economics, University of Calgary.
2. Amy Kapczynski, Professor of Law, Yale Law School, Faculty Co-Director of the Global Health Justice Partnership, and Faculty Co-Director of the Collaboration for Research Integrity and Transparency .
3. Brook Baker, Professor of Law, Northeastern University, School of Law, Research Fellow, University of KwaZulu Natal in Durban, South Africa.
4. Diane Singhroy, PhD, Research Associate, McGill University.
5. Ellen ‘t Hoen, LLM, PhD. Director, Medicines Law & Policy.
6. Fifa Rahman, Board Member Unitaid NGO Delegation and PhD Candidate (International Trade and Intellectual Property), University of Leeds.
7. Gilberto de Lima Lopes Junior, MD, MBA, FAMS, Associate Professor of Clinical Medicine Medical Director for International Programs Associate Director for Global

Oncology Co-Leader, Lung Cancer Site Disease Group Sylvester Comprehensive Cancer Center at the University of Miami and the Miller School of Medicine.

8. Hani Serag, Egyptian Foundation for Health for All
9. Hannes Braberg, Staff Scientist at University of California, San Francisco.
10. Jorge Bermudez, MD, DSc, Head of the Department of Medicines and Pharmaceutical Policies, National School of Public Health/ Oswaldo Cruz Foundation, Member of the UN Secretary-General High-Level Panel on Access to Medicines.
11. Lawrence Gostin, University Professor, Georgetown University, Washington, DC
12. Leeza Osipenko, PhD. Senior Lecturer in Practice, LSE.
13. Margo A. Bagley, Asa Griggs Candler Professor of Law, Emory University School of Law, Faculty Fellow, Emory Global Health Initiative (EGHI), Senior Fellow, Centre for International Governance Innovation (CIGI), Collaborator, Harvard University Global Access in Action (GAiA) Program.
14. Mariana Mazzucato, Professor in the Economics of Innovation and Public Value, University College London; Founder and Director, the UCL Institute for Innovation and Public Purpose.
15. Marie-Paule Kieny, PhD. Director of Research, Institut national de la santé et de la recherche médicale (INSERM), Chair, Drugs for Neglected Diseases Initiative Board of Directors, and Chair, Medicines Patent Pool Foundation Governance Board.
16. Melissa Barber, PhD student, Harvard University.
17. Ophira Ginsburg, Associate Professor, Department of Population Health, New York University School of Medicine.
18. Ravi Ram, Director, RMH Systems, and Independent Health Systems Evaluator, Kenya.
19. Suerie Moon, MPA, PhD. Director of Research at the Global Health Centre, Graduate Institute of International and Development Studies, Geneva and Adjunct Lecturer on Global Health at the Harvard T.H. Chan School of Public Health.
20. William "Terry" W. Fisher III. WilmerHale Professor of Intellectual Property Law at Harvard Law School and Faculty Director of the Berkman Center for Internet and Society.

From: Bleimund, Emily (OS/OGA) [Emily.Bleimund@hhs.gov]
Sent: 4/7/2020 8:47:29 PM
To: Ferriter, Karin [Karin.Ferriter@USPTO.GOV]; b6 @state.gov]; b6
b6 @state.gov]; b6 @state.gov]; Burr, Mara (HHS/OS/OGA)
[/o=ExchangeLabs/ou=Exchange Administrative Group
(FYDIBOHF23SPDLT)/cn=Recipients/cn=502715995a8e4b188f4d215be38756f1-Mara.Burr.O b6
b6 @state.gov]; b6 @state.gov]; b6 @state.gov]; b6
b6 @state.gov]; Perlmutter, Shira [Shira.Perlmutter@USPTO.GOV]; Critharis, Mary
[Mary.Critharis@USPTO.GOV]; Moezie, Minna F. [Minna.Moezie@USPTO.GOV]; b6
b6 @state.gov]; b6 @state.gov]; Grazier, Nyeemah [Nyeemah.Grazier@USPTO.GOV];
Saha, Soma [Soma.Saha@USPTO.GOV]; b6 @state.gov]; Stewart, Coke
[Coke.Stewart@uspto.gov]; Donis, Ruben (OS/ASPR/BARDA) [/o=ExchangeLabs/ou=Exchange Administrative Group
(FYDIBOHF23SPDLT)/cn=Recipients/cn=b3f6ffc6931a4d7fabeeffea4ac27b9d-Ruben.Donis]; Johnson, Robert
(OS/ASPR/BARDA) [/o=ExchangeLabs/ou=Exchange Administrative Group
(FYDIBOHF23SPDLT)/cn=Recipients/cn=feb0b05457404e2f8b88af78e9ac4dd9-Robert.John]; Rohrbaugh, Mark
(NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group
(FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; b6
(STATE.GOV) b6 @state.gov]; b6 @state.gov]; Dixton, Jennifer (ATR)
b6 Taylor, Yair (ATR b6 Wood, Rachel (HHS/OS/OGA)
[/o=ExchangeLabs/ou=Exchange Administrative Group
(FYDIBOHF23SPDLT)/cn=Recipients/cn=de0301e4b65f4fd28f00a5a97bec424b-Rachel.Wood]; Snyder, Anne
(HHS/OS/OGA) [/o=ExchangeLabs/ou=Exchange Administrative Group
(FYDIBOHF23SPDLT)/cn=Recipients/cn=9ebb46d509b9437dac550d81d1dbc5ee-Anne.Berlow]; OGA PET-GHSA Team
[OGAPET-GHSATeam@hhs.gov]; Lamourelle, Gabrielle (HHS/OS/OGA) [/o=ExchangeLabs/ou=Exchange
Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=217e0bf8b30b4548b8e2df338e59f156-Gabrie.Lamo];
b6 @state.gov]; cabbott@usaid.gov; Wubbenhorst, Monique C. (GH/AA)
[mwubbenhorst@usaid.gov]; Holohan, Meghan (PPL/DE) [mholohan@usaid.gov]; b6
b6 Abdoo, Mark (FDA/OC)
[/o=ExchangeLabs/ou=Exchange Administrative Group
(FYDIBOHF23SPDLT)/cn=Recipients/cn=7eafb9b302054654ac154a0a334cc0a5-Mark.Abdoo.];
b6 Ferguson, Steve (NIH/OD)
[E] [/o=ExchangeLabs/ou=Exchange Administrative Group
(FYDIBOHF23SPDLT)/cn=Recipients/cn=aec79b088ce947819eadd4bf420aa54b-fergusos]
CC: Ayala, Ana (OS/ASPR/SPPR) [/o=ExchangeLabs/ou=Exchange Administrative Group
(FYDIBOHF23SPDLT)/cn=Recipients/cn=3e0fc4a1ec874af094a85aa0d6fcc300-Ana.Ayala.O]; Weinberger, Collin
(OS/OGA) [/o=ExchangeLabs/ou=Exchange Administrative Group
(FYDIBOHF23SPDLT)/cn=Recipients/cn=36a1fa70b9f94ec49f3757da88df1364-Collin.Wein]; Aasen, Adam
(HHS/OS/OGA) [/o=ExchangeLabs/ou=Exchange Administrative Group
(FYDIBOHF23SPDLT)/cn=Recipients/cn=b984c46d0b7242599597a50498827f35-Adam.Aasen.]; Ferrey, Seth
(OS/OGA) [/o=ExchangeLabs/ou=Exchange Administrative Group
(FYDIBOHF23SPDLT)/cn=Recipients/cn=a3a078d59c624c9b98f3d7928874954b-Seth.Ferrey]; Mitchell, Stevan
[Stevan.Mitchell@trade.gov]; Ranjan, Mukul (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group
(FYDIBOHF23SPDLT)/cn=Recipients/cn=581507f5b19448408e379fab80b9f849-mranjan]; Galloway, Summer
(CDC/DDID/NCIRD/ID) [/o=ExchangeLabs/ou=Exchange Administrative Group
(FYDIBOHF23SPDLT)/cn=Recipients/cn=a4b7bab0c866407daf1300fac6b527c9-nmd3]; Chandrasekera, Ruvani
(OS/ASPR/SPPR) [/o=ExchangeLabs/ou=Exchange Administrative Group
(FYDIBOHF23SPDLT)/cn=Recipients/cn=25212119902f4c1485064c6ed54d6f18-Ruvani.Chan]
Subject: RE: IP and Health discussion
Attachments: KEI-PC-Congress-CostaRica-26March2020.pdf

See attached the letter from KEI to Congress

Emily Bleimund, JD, MA
Director, Trade and Health

Office of Global Affairs
U.S. Department of Health and Human Services
202-691-2188
Mobile: b6
www.hhs.gov/global

-----Original Appointment-----
From: Ferriter, Karin <Karin.Ferriter@USPTO.GOV>
Sent: Tuesday, April 7, 2020 11:12 AM
To: Ferriter, Karin b6 Bleimund, Emily (OS/OGA) b6 urr, Mara (HHS/OS/OGA) b6 Perlmutter, Shira; Critharis, Mary; Moezie, Minna F. b6 Grazier, Nyeemah; Saha, Soma; b6 Stewart, Coke; Donis, Ruben (OS/ASPR/BARDA); Johnson, Robert (OS/ASPR/BARDA); Rohrbaugh, Mark (NIH/OD) [E] b6 (STATE.GOV); b6 Wood, Rachel (HHS/OS/OGA); Snyder, Anne (HHS/OS/OGA); OGA PET-GHSA Team; Lamourelle, Gabrielle (HHS/OS/OGA); Tracy Carson; cabbott@usaid.gov; Wubbenhorst, Monique C. (GH/AA); Holohan, Meghan (PPL/DE) b6 b6 Abdoo, Mark (FDA/OC) b6 b6 Ferguson, Steve (NIH/OD) [E]
Cc: Ayala, Ana (OS/ASPR/SPPR); Weinberger, Collin (OS/OGA); Aasen, Adam (HHS/OS/OGA); Ferrey, Seth (OS/OGA); Mitchell, Stevan; Ranjan, Mukul (NIH/NIAID) [E]; Galloway, Summer (CDC/DDID/NCIRD/ID); Chandrasekera, Ruvani (OS/ASPR/SPPR)
Subject: IP and Health discussion
When: Tuesday, April 7, 2020 3:30 PM-4:30 PM (UTC-05:00) Eastern Time (US & Canada).
Where: WebEX

This is to compare notes b5 COVID-19, and otherwise within the UN system, as well as to b5

Please email me any other discussion topics and I will circulate an agenda before the call.

I suspect that there will be other calls, so if you or a colleague cannot attend I am confident you will be able to join another time. While you are welcome to forward to others who should join, I also welcome you letting me know who should be on the call so that we have a complete list of staff level IP and Health experts.

Thank you,

Karin Ferriter
Deputy Chief Policy Officer
Office of Policy and International Affairs
USPTO
DO NOT DELETE OR CHANGE ANY OF THE TEXT BELOW THIS LINE

Karin Ferriter has scheduled this WebEx meeting.

IP and Health discussion
Host: Karin Ferriter

When it's time, start or join the WebEx meeting from here:
b6

Access Information

Meeting Number: b6
Meeting Password: b6

Audio Connection

b6 (CWMS Call In)

Access Code:
b6

Hosts, need your host access code or key? Go to the meeting information page:
b6

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March 26, 2020

Senators Mitch McConnell and Charles Schumer
Representatives Nancy Pelosi and Kevin McCarthy

Re: Proposal by the President of Costa Rica to the World Health Organization to create a pool for rights in technology and data related to the prevention, detection and treatment of the coronavirus/COVID-19 pandemic

Dear Senators McConnell and Schumer and Representatives Pelosi and McCarthy

KEI and Public Citizen would like to call your attention to an initiative proposed by the President of Costa Rica, asking the World Health Organization (WHO) to create a global pool of rights in the data, knowledge and technologies useful to the prevention, detection and treatment of the coronavirus/COVID-19 pandemic. [Link] The Director-General of the WHO has since welcomed the proposal, and joined the call for pooled rights. [Link]

Costa Rica correctly saw this as a pool with a diverse set of rights, including those relating to patents on inventions and designs, regulatory test data, and research data including outcomes, know-how, cell lines, copyrights and blueprints for manufacturing, as these rights relate to equipment, diagnostic tests, devices, medicines, vaccines, and other medical tools.

Such a pool would allow for competitive and accelerated production of needed COVID-19 technologies, and expand the global capacity to address the need for affordable products.

The inputs to such a pool could come from governments that fund research and development or buy innovative products, as well as from universities, research institutes, charities, private companies and individuals who control rights.

The United States government is funding a significant amount of COVID-19 research and development, but many other governments around the world, such as Germany, Japan, Canada, France, China, the European Union, the UK and Australia, are also leading efforts. A pool structure could help ensure broader access to rights of R&D funded by other governments. This could result in the quicker national introduction of needed medicines and vaccines, for example.

This is a moment for governments to demonstrate there will be global cooperation in fighting the pandemic. The new coronavirus could continue to pose a threat, with possibilities for mutation and seasonal circulation, unless it is eradicated globally.

In the new funding authority relating to this pandemic, the U.S. will be able to use "Other Transactions Authority" (OTA), as well as other procurement authorities. Among the approaches the United States can take to expand access and increase the supply of products is to use federal funds to buy out patent and data rights, and/or to offer incentives like innovation inducement prices and market entry rewards to delink the incentives for development from the grants of legal monopolies, in order to effectively make the R&D a public good. If well-designed and linked to a reasonable reward, these measures can be very effective in ensuring that products can be made everywhere and sourced at prices that reflect the costs of manufacturing. The benefits of such measures would be global, and the United States can and should encourage other governments to collaborate in paying for patent/data rights buyouts or innovation inducement prizes. Of course, this is just one possible approach to be taken, but it illustrates how it can be in the U.S. interest to engage other governments and even private funders of R&D to work toward the sharing of the costs of public goods.

The Costa Rica proposal is measured, and begins with an initial memorandum of understanding between governments and other entities funding R&D that will enable future assignments of rights, with the opportunity to decide on the specific technologies and terms for assignments later.

Given the need to act quickly, we encourage your office to write Vice President Mike Pence and Secretary of Health and Human Services Alex Azar as soon as practicable, to encourage the United States government to support the Costa Rica proposal.

To be concrete about the next steps, the WHO could be asked to ask funders of R&D and rights holders to sign a very short agreement, as a first step, that reads like this:

.... [Funder, rights holder] agrees to consider requests by the World Health Organization to obtain a limited assignment of rights in U.S. funded patent rights for biomedical inventions related to the detection, prevention or treatment of coronavirus related illnesses for use worldwide in collaboration with its member states. The terms and conditions associated with such an assignment, if so granted, will be determined by the [Funder/Rights holder] The WHO agrees the [Funder/rights holder] is under no obligation to grant any such requests, but only to consider them.

If signed by the United States, this would enable the United States to reference this option in funding agreements, under 35 U.S.C. § 202(c)(4), as well as in CRADAs, Cooperative Agreements, and "Other Transactions Authority" (OTA) agreements.

Moreover, if the U.S. shows leadership on this, it will be far easier for the United States to obtain access to rights in data, including clinical trial test data, inventions and other data and technology rights, funded by others, including foreign governments, many of whom are also mobilizing significant resources for new R&D.

Robert Weissman, Public Citizen James Love, Knowledge Ecology International

---

From: Ferriter, Karin [Karin.Ferriter@USPTO.GOV]
Sent: 4/8/2020 3:34:12 PM
To: Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]
Subject: RE: Response to March 13 KEI Letter

Thank you, Mark. b5

b5

I am trying to understand b5

b5

Sent with BlackBerry Work
(www.blackberry.com)

From: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Date: Wednesday, Apr 08, 2020, 10:57 AM
To: Ferriter, Karin <Karin.Ferriter@USPTO.GOV>
Cc: Bleimund, Emily (OS/OGA) <Emily.Bleimund@hhs.gov>, Moezie, Minna F. <Minna.Moezie@USPTO.GOV>, Lamm, Marina <Marina.Lamm@USPTO.GOV>, Saha, Soma <Soma.Saha@USPTO.GOV>, Grazier, Nyeemah <Nyeemah.Grazier@USPTO.GOV>
Subject: RE: Response to March 13 KEI Letter

NIH b5

b5

From: Ferriter, Karin <Karin.Ferriter@USPTO.GOV>
Sent: Wednesday, April 8, 2020 9:07 AM
To: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Cc: Bleimund, Emily (OS/OGA) <Emily.Bleimund@hhs.gov>; Moezie, Minna F. <Minna.Moezie@USPTO.GOV>; Lamm, Marina <Marina.Lamm@USPTO.GOV>; Saha, Soma <Soma.Saha@USPTO.GOV>; Grazier, Nyeemah <Nyeemah.Grazier@USPTO.GOV>
Subject: RE: Response to March 13 KEI Letter

Should we b5 Also, b5

b5

b5

I defer to you all- you are the experts, but if there is b5 that would be great.

Karin

From: Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>
Sent: Tuesday, April 7, 2020 4:55 PM
To: Ferriter, Karin <Karin.Ferriter@USPTO.GOV>; Bleimund, Emily (OS/OGA) <Emily.Bleimund@hhs.gov>
Subject: FW: Response to March 13 KEI Letter

FYI. Letter from KEI to Sec. Azar about using particular Bayh-Dole authorities including an agreement with WHO to assign patent rights to them. My response is an acknowledgement.

From: SciencePolicy <SciencePolicy@od.nih.gov>
Sent: Monday, April 6, 2020 1:30 PM
To: james.love@keionline.org
Subject: Response to March 13 KEI Letter

Dear Mr. Love,

Attached, please see the response to your March 13, 2020, letter to the Secretary of Health and Human Services, Alex Azar.

Thanks
Ryan

Ryan T. Bayha
Director of Strategic Engagement
Office of Science Policy
National Institutes of Health
6705 Rockledge Drive, Suite 750
Bethesda, MD 20892
301- 496-9838 (p)
301-496-9838 (f)

From: Dixton, Jennifer (ATR) b6
Sent: 4/7/2020 11:00:48 PM
To: Ferriter, Karin [Karin.Ferriter@USPTO.GOV]; Bleimund, Emily (OS/OGA) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=343f92b5144f4c59a3cfc177522a7a79-Emily.Bleim]; b5 @state.gov]; b5 @state.gov]; b5 b5 @state.gov]; Burr, Mara (HHS/OS/OGA) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=502715995a8e4b188f4d215be38756f1-Mara.Burr.O]; b5 b5 @state.gov]; b5 @state.gov]; b5 @state.gov]; b5 b5 @state.gov]; Perlmutter, Shira [Shira.Perlmutter@USPTO.GOV]; Critharis, Mary [Mary.Critharis@USPTO.GOV]; Moezie, Minna F. [Minna.Moezie@USPTO.GOV]; b5 b5 tate.gov]; b5 @state.gov]; Grazier, Nyeemah [Nyeemah.Grazier@USPTO.GOV]; Saha, Soma [Soma.Saha@USPTO.GOV]; b5 @state.gov]; Stewart, Coke [Coke.Stewart@uspto.gov]; Donis, Ruben (OS/ASPR/BARDA) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b3f6ffc6931a4d7fabeeffea4ac27b9d-Ruben.Donis]; Johnson, Robert (OS/ASPR/BARDA) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=feb0b05457404e2f8b88af78e9ac4dd9-Robert.John]; Rohrbaugh, Mark (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=591ab6b2424b4b8997082718cbb29fab-rohrbaum]; b5 (STATE.GOV) b5 @state.gov]; b5 @state.gov]; Taylor, Yair (ATR) b6 Wood, Rachel (HHS/OS/OGA) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=de0301e4b65f4fd28f00a5a97bec424b-Rachel.Wood]; Snyder, Anne (HHS/OS/OGA) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9ebb46d509b9437dac550d81d1dbc5ee-Anne.Berlow]; OGA PET-GHSA Team [OGAPET-GHSATeam@hhs.gov]; Lamourelle, Gabrielle (HHS/OS/OGA) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=217e0bf8b30b4548b8e2df338e59f156-Gabrie.Lamo]; b5 @state.gov]; cabbott@usaid.gov; Wubbenhorst, Monique C. (GH/AA) [mwubbenhorst@usaid.gov]; Holohan, Meghan (PPL/DE) [mholohan@usaid.gov] b6 b6 Abdoo, Mark (FDA/OC) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7eafb9b302054654ac154a0a334cc0a5-Mark.Abdoo.]; b6 Ferguson, Steve (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=aec79b088ce947819eadd4bf420aa54b-fergusos]
CC: Ayala, Ana (OS/ASPR/SPPR) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3e0fc4a1ec874af094a85aa0d6fcc300-Ana.Ayala.O]; Weinberger, Collin (OS/OGA) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=36a1fa70b9f94ec49f3757da88df1364-Collin.Wein]; Aasen, Adam (HHS/OS/OGA) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b984c46d0b7242599597a50498827f35-Adam.Aasen.]; Ferrey, Seth (OS/OGA) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a3a078d59c624c9b98f3d7928874954b-Seth.Ferrey]; Mitchell, Stevan [Stevan.Mitchell@trade.gov]; Ranjan, Mukul (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=581507f5b19448408e379fab80b9f849-mranjan]; Galloway, Summer (CDC/DDID/NCIRD/ID) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a4b7bab0c866407daf1300fac6b527c9-nmd3]; Chandrasekera, Ruvani (OS/ASPR/SPPR) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=25212119902f4c1485064c6ed54d6f18-Ruvani.Chan]
Subject: RE: IP and Health discussion

Also, please note the DOJ's and FTC's expedited business review procedure that I mentioned in the call -- in the event companies have concerns that a collaboration raises antitrust issues:
https://www.justice.gov/atr/joint-antitrust-statement-regarding-covid-19

Jennifer M. Dixton
Special Counsel for Policy & Intellectual Property
U.S. Department of Justice | Antitrust Division | Competition Policy & Advocacy Section

209 South LaSalle, Suit b6
Chicago, IL 60604
b6 Office) b6 Mobile)
b6

From: Ferriter, Karin <Karin.Ferriter@USPTO.GOV>
Sent: Tuesday, April 7, 2020 5:50 PM
To: Bleimund, Emily (OS/OGA) <Emily.Bleimund@hhs.gov>; b5 @state.gov>; b5 b5 @state.gov>; b5 @state.gov>; Burr, Mara (HHS/OS/OGA) <Mara.Burr@hhs.gov>; b5 @state.gov>; b5 @state.gov>; b5 b5 @state.gov>; b5 @state.gov>; Perlmutter, Shira <Shira.Perlmutter@USPTO.GOV>; Critharis, Mary <Mary.Critharis@USPTO.GOV>; Moezie, Minna F. <Minna.Moezie@USPTO.GOV>; b5 @state.gov>; b5 @state.gov>; Grazier, Nyeemah <Nyeemah.Grazier@USPTO.GOV>; Saha, Soma <Soma.Saha@USPTO.GOV>; b5 b5 @state.gov>; Stewart, Coke <Coke.Stewart@uspto.gov>; Donis, Ruben (OS/ASPR/BARDA) <Ruben.Donis@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; b5 (STATE.GOV) b5 @state.gov>; b5 OS) b5 @state.gov>; Dixton, Jennifer (ATR) < b6 Taylor, Yair (ATR) b6 Wood, Rachel (HHS/OS/OGA) <Rachel.Wood@hhs.gov>; Snyder, Anne (HHS/OS/OGA) <Anne.Snyder@hhs.gov>; OGA PET-GHSA Team <OGAPET-GHSATeam@hhs.gov>; Lamourelle, Gabrielle (HHS/OS/OGA) <Gabrielle.Lamourelle@hhs.gov>; b5 @state.gov>; cabbott@usaid.gov; Wubbenhorst, Monique C. (GH/AA) <mwubbenhorst@usaid.gov>; Holohan, Meghan (PPL/DE) <mholohan@usaid.gov>; b6 b6 Abdoo, Mark (FDA/OC) <Mark.Abdoo@fda.hhs.gov>; b6 Ferguson, Steve (NIH/OD) [E] <fergusos@od6100m1.od.nih.gov>
Cc: Ayala, Ana (OS/ASPR/SPPR) <Ana.Ayala@hhs.gov>; Weinberger, Collin (OS/OGA) <Collin.Weinberger@hhs.gov>; Aasen, Adam (HHS/OS/OGA) <Adam.Aasen@hhs.gov>; Ferrey, Seth (OS/OGA) <Seth.Ferrey@hhs.gov>; Mitchell, Stevan <Stevan.Mitchell@trade.gov>; Ranjan, Mukul (NIH/NIAID) [E] <mranjan@niaid.nih.gov>; Galloway, Summer (CDC/DDID/NCIRD/ID) <nmd3@cdc.gov>; Chandrasekera, Ruvani (OS/ASPR/SPPR) <Ruvani.Chandrasekera@hhs.gov>
Subject: RE: IP and Health discussion

Sorry for all the emails. I left out another action that the USG is supporting- it could be the most important one:

> Governments share their international health regulation reporting with each other rather than just with the WHO so that there is a quicker reporting

---

From: Ferriter, Karin
Sent: Tuesday, April 7, 2020 6:38 PM
To: Bleimund, Emily (OS/OGA) <Emily.Bleimund@hhs.gov>; b5 @state.gov>; b5 b5 @state.gov>; b5 @state.gov>; Burr, Mara (HHS/OS/OGA) <Mara.Burr@hhs.gov>; b5 @state.gov>; b5 @state.gov>; b5 b5 @state.gov>; b5 @state.gov>; Perlmutter, Shira <Shira.Perlmutter@USPTO.GOV>; Critharis, Mary <Mary.Critharis@USPTO.GOV>; Moezie, Minna F. <Minna.Moezie@USPTO.GOV>; b5 @state.gov>; b5 @state.gov>; Grazier, Nyeemah <Nyeemah.Grazier@USPTO.GOV>; Saha, Soma <Soma.Saha@USPTO.GOV>; b5 b5 @state.gov>; Stewart, Coke <Coke.Stewart@uspto.gov>; Donis, Ruben (OS/ASPR/BARDA) <Ruben.Donis@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; b5 (STATE.GOV) b5 @state.gov>; b5 OS) b5 @state.gov>; Dixton, Jennifer (ATR) b6 Taylor, Yair (ATR) b6 Wood, Rachel (HHS/OS/OGA) <Rachel.Wood@hhs.gov>; Snyder, Anne (HHS/OS/OGA) <Anne.Snyder@hhs.gov>; OGA PET-GHSA Team <OGAPET-GHSATeam@hhs.gov>; Lamourelle, Gabrielle (HHS/OS/OGA) <Gabrielle.Lamourelle@hhs.gov>; b5 @state.gov>; cabbott@usaid.gov; Wubbenhorst, Monique C.

(GH/AA) <mwubbenhorst@usaid.gov>; Holohan, Meghan (PPL/DE) <mholohan@usaid.gov> b6 b6 Abdoo, Mark (FDA/OC) <Mark.Abdoo@fda.hhs.gov> b6 Ferguson, Steve (NIH/OD) [E] <fergusos@od6100m1.od.nih.gov>
Cc: Ayala, Ana (OS/ASPR/SPPR) <Ana.Ayala@hhs.gov>; Weinberger, Collin (OS/OGA) <Collin.Weinberger@hhs.gov>; Aasen, Adam (HHS/OS/OGA) <Adam.Aasen@hhs.gov>; Ferrey, Seth (OS/OGA) <Seth.Ferrey@hhs.gov>; Mitchell, Stevan <Stevan.Mitchell@trade.gov>; Ranjan, Mukul (NIH/NIAID) [E] <mranjan@niaid.nih.gov>; Galloway, Summer (CDC/DDID/NCIRD/ID) <nmd3@cdc.gov>; Chandrasekera, Ruvani (OS/ASPR/SPPR) <Ruvani.Chandrasekera@hhs.gov>
Subject: RE: IP and Health discussion

Thanks, Emily! Thank you to those who were able to join the call.

Additional reading material: https://www.iam-media.com/coronavirus/the-key-covid-19-compulsory-licensing-developments-so-far

This was my list of actions that the USG and others are strongly supporting (please let the group know if any important ones are omitted):

i. That the USG is being proactive in promoting private sector voluntary licensing to manufacture needed products. A few examples,

    Airon, Ford and GE healthcare is a voluntary partnership, subsequent to President Trump's encouragement to increase ventilator production. https://www.washingtonpost.com/business/2020/04/04/ventilators-coronavirus-ford-gm/

    Amgen is aiming to develop a new drug to treat and prevent COVID-19, using insights from Seattle-based Adaptive Biotechnologies' system for sequencing the human immune system, under an expanded partnership. They began work immediately, even before finalizing financial details and other terms of the partnership. Adaptive says it will use its platform to identify naturally occurring antibodies in the immune systems of COVID-19 survivors, by analyzing blood samples to find antibodies that neutralize the SARS-CoV-2 virus that causes the disease. https://www.geekwire.com/2020/search-covid-19-cure-amgen-adaptive-biotech-partner-quest-new-drug/

    Pfizer Inc. is teaming up with BioNTech SE for the co-development and distribution of a coronavirus vaccine. https://www.forbes.com/sites/jimvinoski/2020/03/17/pfizer-joins-forces-with-biontech-for-covid-19-vaccine-co-development/%234438f88666f6/#61653f9017e8

    IFPMA has listed a number of pharmaceutical and biotech partnerships here: https://www.ifpma.org/subtopics/novel-coronavirus-covid-19-industrys-rd-efforts/

ii. The United States is making information available, including about scams and fraud https://www.epa.gov/coronavirus and https://www.usa.gov/coronavirus

iii. The USG is supporting access to research, including copyrighted works and data
Public Health Emergency COVID-19 Initiative, supported by the National Science and Technology Advisors from a dozen countries: https://www.ncbi.nlm.nih.gov/pmc/about/covid-19/
Elsevier: Coronavirus (COVID-19) Toolkit and other resources
https://www.elsevier.com/clinical-solutions/covid-19-toolkit and
https://www.elsevier.com/connect/coronavirus-initiatives

Copyright Clearance Center's list of Links to COVID-19 Resources
https://www.copyright.com/coronavirus-covid-19/
https://www.weforum.org/agenda/2020/03/how-are-companies-responding-to-the-coronavirus-crisis-d15bed6137
Department of Energy Resources Supporting Coronavirus Research
https://science.osti.gov/DOE-Resources-Supporting-Coronavirus-Research

iv. The USG is supporting access to clinical trial data
https://www.clinicaltrials.gov/

v. The USG is making research funding available and supporting research
   i. Compiled here: https://hub.jhu.edu/novel-coronavirus-information/research-preparedness/research-preparedness-covid-19-funding-opportunities/, including: https://www.nih.gov/grants-funding and https://www.nsf.gov/pubs/2020/nsf20052/nsf20052.jsp
   ii. https://wellcome.ac.uk/grant-funding/schemes/epidemic-preparedness-covid-19 (closed to new expressions of interest)
   iii. https://www.phe.gov/emergency/events/COVID19/Pages/BARDA.aspx

   On the call, there was a question b5
   b5

vi. COVID-19 High Performance Computing Consortium is making high performance computers available for COVID-19 research
https://covid19-hpc-consortium.org/

vii. Genetic Sequences, Isolates, etc are being shared
https://www.gisaid.org/ and https://www.ncbi.nlm.nih.gov/genbank/

viii. The USG and the private sector are providing aid
https://www.usaid.gov/coronavirus
https://www.uschamberfoundation.org/aid-event/corporate-aid-tracker-covid-19-business-action
https://phrma.org/Coronavirus/PhRMA-Member-Efforts

From: Bleimund, Emily (OS/OGA) <Emily.Bleimund@hhs.gov>
Sent: Tuesday, April 7, 2020 4:47 PM
To: Ferriter, Karin <Karin.Ferriter@USPTO.GOV>; b6 @state.gov>; b6 b6 @state.gov>; b6 @state.gov>; Burr, Mara (HHS/OS/OGA) <Mara.Burr@hhs.gov>; b6 @state.gov>; b6 @state.gov>; b5 b5 @state.gov>; b5 @state.gov>; Perlmutter, Shira <Shira.Perlmutter@USPTO.GOV>; Critharis, Mary <Mary.Critharis@USPTO.GOV>; Moezie, Minna F. <Minna.Moezie@USPTO.GOV>; b5 @state.gov>; b5 @state.gov>; Grazier, Nyeemah <Nyeemah.Grazier@USPTO.GOV>; Saha, Soma <Soma.Saha@USPTO.GOV>; b6 b6 @state.gov>; Stewart, Coke <Coke.Stewart@uspto.gov>; Donis, Ruben (OS/ASPR/BARDA) <Ruben.Donis@hhs.gov>; Johnson, Robert (OS/ASPR/BARDA) <Robert.Johnson@hhs.gov>; Rohrbaugh, Mark (NIH/OD) [E] <rohrbaum@od.nih.gov>; b6 (STATE.GOV) b6 @state.gov>; b6 OS) b6 @state.gov>; Dixton, Jennifer (ATR) b6 Taylor, Yair (ATR) b6 Wood, Rachel (HHS/OS/OGA) <Rachel.Wood@hhs.gov>; Snyder, Anne (HHS/OS/OGA)

<Anne.Snyder@hhs.gov>; OGA PET-GHSA Team <OGAPET-GHSATeam@hhs.gov>; Lamourelle, Gabrielle (HHS/OS/OGA) <Gabrielle.Lamourelle@hhs.gov>; b6 @state.gov>; cabbott@usaid.gov; Wubbenhorst, Monique C. (GH/AA) <mwubbenhorst@usaid.gov>; Holohan, Meghan (PPL/DE) <mholohan@usaid.gov>; b6 b6 Abdoo, Mark (FDA/OC) <Mark.Abdoo@fda.hhs.gov>; b6 Ferguson, Steve (NIH/OD) [E] <fergusos@od6100m1.od.nih.gov>
Cc: Ayala, Ana (OS/ASPR/SPPR) <Ana.Ayala@hhs.gov>; Weinberger, Collin (OS/OGA) <Collin.Weinberger@hhs.gov>; Aasen, Adam (HHS/OS/OGA) <Adam.Aasen@hhs.gov>; Ferrey, Seth (OS/OGA) <Seth.Ferrey@hhs.gov>; Mitchell, Stevan <Stevan.Mitchell@trade.gov>; Ranjan, Mukul (NIH/NIAID) [E] <mranjan@niaid.nih.gov>; Galloway, Summer (CDC/DDID/NCIRD/ID) <nmd3@cdc.gov>; Chandrasekera, Ruvani (OS/ASPR/SPPR) <Ruvani.Chandrasekera@hhs.gov>
Subject: RE: IP and Health discussion

See attached the letter from KEI to Congress

Emily Bleimund, JD, MA
Director, Trade and Health
Office of Global Affairs
U.S. Department of Health and Human Services
b6
Mobile: b6
www.hhs.gov/global

-----Original Appointment-----
From: Ferriter, Karin <Karin.Ferriter@USPTO.GOV>
Sent: Tuesday, April 7, 2020 11:12 AM
To: Ferriter, Karin; b6 Bleimund, Emily (OS/OGA); b6 Burr, Mara (HHS/OS/OGA); b6 b5 Perlmutter, Shira; Critharis, Mary; Moezie, Minna F.; b5 Grazier, Nyeemah; Saha, Soma; b6 Stewart, Coke; Donis, Ruben (OS/ASPR/BARDA); Johnson, Robert (OS/ASPR/BARDA); Rohrbaugh, Mark (NIH/OD) [E] b6 (STATE.GOV) b6 OS); Dixton, Jennifer (ATR); Taylor, Yair (ATR); Wood, Rachel (HHS/OS/OGA); Snyder, Anne (HHS/OS/OGA); OGA PET-GHSA Team; Lamourelle, Gabrielle (HHS/OS/OGA); b6 cabbott@usaid.gov; Wubbenhorst, Monique C. (GH/AA); Holohan, Meghan (PPL/DE) b6 b6 Abdoo, Mark (FDA/OC); b6 b6 Ferguson, Steve (NIH/OD) [E]
Cc: Ayala, Ana (OS/ASPR/SPPR); Weinberger, Collin (OS/OGA); Aasen, Adam (HHS/OS/OGA); Ferrey, Seth (OS/OGA); Mitchell, Stevan; Ranjan, Mukul (NIH/NIAID) [E]; Galloway, Summer (CDC/DDID/NCIRD/ID); Chandrasekera, Ruvani (OS/ASPR/SPPR)
Subject: IP and Health discussion
When: Tuesday, April 7, 2020 3:30 PM-4:30 PM (UTC-05:00) Eastern Time (US & Canada).
Where: WebEX

This is to compare notes b5 COVID-19, and otherwise within the UN system, as well as to b5

Please email me any other discussion topics and I will circulate an agenda before the call.

I suspect that there will be other calls, so if you or a colleague cannot attend I am confident you will be able to join another time. While you are welcome to forward to others who should join, I also welcome you letting me know who should be on the call so that we have a complete list of staff level IP and Health experts.

Thank you,

Karin Ferriter
Deputy Chief Policy Officer
Office of Policy and International Affairs
USPTO
DO NOT DELETE OR CHANGE ANY OF THE TEXT BELOW THIS LINE

Karin Ferriter has scheduled this WebEx meeting.

IP and Health discussion
Host: Karin Ferriter

When it's time, start or join the WebEx meeting from here:
b6

Access Information

Meeting Number: b6
Meeting Password: b6

Audio Connection

b6 (CWMS Call In)

Access Code:
b6

Hosts, need your host access code or key? Go to the meeting information page:
b6

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